Small, Non-Isomorpic, Strongly Balanced, Uniform Repeated Measures (Cross-Over) Designs.

by

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The ruddy glow of sunset was already fading into the sombre shadows of night, when two travellers might have been observed swiftly - at a pace of six miles in the hour - descending the rugged side of a mountain; the younger bounding from crag to crag with the agility of a fawn, while the his companion, whose aged limbs seemed ill at ease in the heavy chain armour habitually worn by tourists in the district, toiled on painfully at his side.

As is always the case under such circumstances, the younger knight was the first to break the silence.

"A goodly pace, I trow!" he explained. "We sped not thus in the ascent!"

"Goodly, indeed!" the other echoed with a groan. "We clomb it but at three miles in the hour."

"And on the dead level our pace is — ?" the younger suggested; for he was weak in statistics, and left all such details to his aged companion.

"Four miles in the hour," the other wearily replied. "Not an ounce more," he added, with that love of metaphor so common in old age, "and not a farthing less!"

" 'Twas three hours past high noon when we left our hostelry," the young man said, musingly. "We shall scarce be back by supper-time. Perchance mine host will roundly deny us all food!"

"He will chide our tardy return," was the grave reply, "and such a rebuke will be meet."

"A brave conceit!" cried the other, with a merry laugh. "And should we bid him bring us yet another course, I trow his answer will be tart!"

"We shall but get our deserts," sighed the elder knight, who had never seen a joke in his life, and was somewhat displeased at his companions' untimely levity. " 'Twill be nine of the clock," he added in an undertone, "by the time we regain our hostelry. Full many a mile shall we have plodded this day!"

"How many? How many?" cried the eager youth, ever athirst for knowledge.

The old man was silent.

"Tell me," he answered, after a moment's thought, "what time it was when we stood together on yonder peak. Not exact to the minute!" he added hastily, reading the protest in the young man's face. "An' thy guess be within one poor half-hour of the mark, 'tis all I ask of thy mother's son! Then will I tell thee true to the last inch, how far we shall have trudged betwixt three and nine of the clock."

A groan was the young man's only reply; while his convulsed features and the deep wrinkles that chased each other across his manly brow, revealed the abyss of arithmetical agony into which one chance question had plunged him.

Lewis Carroll
A Tangled Tale Knot I

Contents

Abstract

This thesis is concerned with the construction of strongly balanced, uniform repeated measures designs, for a small number of treatments, periods, and experimental units.

Experiments using units, or subjects, where more than one treatment is applied to each unit, although at different periods in time, and the subjects' response is measured at each of these times, are known as *repeated measures designs* (RMDs), carry-over or cross-over designs. They are used when there are not enough subjects to have only one treatment per subject or when a within subject effect of treatment is to be estimated. Typically they are used for animal feeding trials and in clinical trials.

In repeated measures designs there can be carry-over or residual treatment effects, since more than one treatment is used per subject. To overcome this, it may be necessary to have a suitable length of time between treatments. This is known as a *washout period*. Despite this, it is not always possible to overcome earlier treatment effects, either due to the nature of the treatments or because too long a time period would be required. This could mean that the conditions under which the experiment is being run are no longer homogeneous. In this case it is necessary to consider residual treatment effects in the linear model to allow for the inadequacy, or more commonly the absence, of washout periods.

Williams (1949), among others, considered construction of designs taking residual effects into account. His designs have each treatment following all other treatments the same number of times; these designs are known as *balanced repeated measures designs*. Using these designs, estimates of all effects can be obtained, however, the disadvantage of these designs is that a treatment never follows itself in a design, and as such they are not as efficient in estimating residual treatment effects.

However, from the literature it can be shown that designs that have each treatment appearing the same number of times for each subject and each period and have all treatments followed by all other treatments (including itself) the same number of times are 'best' in the estimation of direct treatment effects and of residual treatment effects. These are known as *strongly balanced, uniform repeated measures designs* (SBURMDs). The known constructions of SBURMDs are summarised and other non-isomorphic designs belonging to this class are constructed here. Hence a design can be chosen from a set of possible designs.

This thesis aims to find all non-isomorphic SBURMDs for small numbers of treatments, periods, and experimental units, and to form general constructions for the whole class of these designs, and to make general comments about these designs based on the known properties of RMDs for the given linear models.

Signed Statement

This thesis contains no material which has been accepted for the award of any other degree or diploma in any University and that, to the best of my knowledge and belief, it contains no material previously published or written by another person, except where due reference is made in the text of the thesis.

I consent to the thesis being made available for photocopying and loan if it is accepted for the award of the degree.

Sandra Pattison

August 5, 1991.

I have already submitted some parts of this work for publication. Section 2.3.2 , and Sections 1,2 and 3 of Chapter 3 appeared in Pattison and Street (1990), (see Appendix N). Part of Section 4.1.1 on Symmetric SBURMDs for t=3 was done jointly with Deborah J. Street and appears in Pattison and Street (1990).

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List of Tables

Abbreviations

RMD	Repeated measures design
RMD(t,n,p)	Repeated measures design with t treatments, n subjects and p periods
SBRMD	Strongly balanced repeated measures design
SBURMD	Strongly balanced, uniform repeated measures design
BRMD	Balanced repeated measures design
BURMD	Balanced, uniform repeated measures design
CRMD	Circular repeated measures design
CSBURMD	Circular, strongly balanced, uniform repeated measures design

Chapter 1 Introduction and Repeated Measures Designs in General

1.1 Introduction

Experiments using units, or subjects, where more than one treatment is applied to each unit, although at different periods in time, and the subjects' response is measured at each of these times, are known as *repeated measures designs* (RMDs), *carry-over* or *cross-over designs* (see Jones and Kenward (1989) for an introduction). These designs should be distinguished from growth curve designs, which are sometimes called repeated measurements designs, where the response of a subject is measured more than once but with only one treatment applied, usually at the beginning of the experiment.

Repeated measures designs are used when there are not enough subjects to have only one treatment per subject or when a within-subject effect of treatment is to be estimated. Typically they have been used for animal feeding trials and clinical trials. Examples of feeding trials can be found in Hovell, Ngambi, Barber and Kyle (1986), Wilkinson, Cole and Lewis (1982), Castle and Watson (1982), and John and Quenouille (1977, pp. 211-214). Examples of clinical trials can be found in Bassein, Borghi, Costa, Stocchi, Mussi and Umbrosioni (1985), Parkes (1982), and Thornton, Smith and Kissileff (1987). Other examples of the application of repeated measures designs, in areas such as bioassays and industry, can be found in Finney (1956) and Raghavarao (1990) respectively.

As an example, Thornton *et al.*, (1987) described an experiment designed to see if a synthetic octapeptide reduced food intake. Twelve male subjects were intravenously given either a Saline solution (Placebo) or a Synthetic Octapeptide of Cholecystokin (CCK-8), on each of four non-consecutive days whilst eating a test meal, with food intake measured as the response. This is a repeated measures design with twelve experimental units, two treatments and four periods, where the response variate is food intake. The design is represented by the six sequences in Table 1.1-1, each sequence being used for two subjects.

Sequence		1	2	3	4	5	6
Period	1 (Day 1)	CCK-8	CCK-8	CCK-8	Placebo	Placebo	Placebo
	2 (Day 3)	CCK-8	Placebo	Placebo	CCK-8	CCK-8	Placebo
	3 (Day 5)	Placebo	Placebo	CCK-8	Placebo	CCK-8	CCK-8
	4 (Day 7)	Placebo	CCK-8	Placebo	CCK-8	Placebo	CCK-8

Table 1.1-1: *The six sequences used to see if CCK-8 reduced food intake.*

In repeated measures designs there can be carry-over, or residual, treatment effects as more than one treatment is used per subject. To overcome this effect, it may be necessary to have a suitable length of time between treatments. This is known as a *washout period.* Despite this, it is not always possible to overcome earlier treatment effects, either due to the nature of the treatments or because too long a time period would be required. This could mean that the conditions under which the experiment are being run are no longer homogeneous. In this case it is necessary to consider residual treatment effects in a linear model to allow for the inadequacy, or more commonly absence, of washout periods. If an allowance is not made for these effects then the treatment estimates may be biased.

The example in Table 1.1-1 has one day between the application of successive treatments. This may not be long enough to 'washout' the previous treatment, so a residual treatment effect from the previous period needs to be considered, in addition to the treatment effect and effects due to subject and period.

This thesis is concerned with linear models for repeated measures designs, where the model takes into account a residual treatment effect of the previous period as well as the direct treatment effect. Williams (1949), among others, considered construction of designs taking residual effects into account. These designs are known as *balanced repeated measures designs* and have each treatment following all other treatments the same number of times in any given design. A review of designs that have this property and have treatments appearing the same number of times in each subject and period appear in Hedayat and Afsarinejad (1975). The disadvantage of these designs is that a treatment never follows itself in a design, and as such it is not as efficient in estimating residual effects.

However, in the review of the literature in Chapter 2 we see that designs that have each treatment appearing the same number of times for each subject and each period and have all treatments followed by all other treatments (including itself) the same number of times are 'best' in the estimation of direct treatment effects and of residual treatment effects. Quenouille (1953), Berenblut (1964), Patterson (1970, 1973), Kok and Patterson (1976), Cheng and Wu (1980) and Sen and Mukerjee (1987) give particular designs or methods of constructions of families of designs with these properties. These are also discussed in Chapter 2.

There are, however, other designs belonging to this class that could be used but cannot be constructed by these methods. This thesis aims to find all designs which are 'best' in the estimation of direct and residual treatment effects, and to form general constructions for the whole class of these designs. These constructions are presented in Chapters 3 and 4 for small numbers of treatments. The differences between these designs are also investigated, which may lead to randomly selecting a design from a subset of all the possible designs in this class.

Initially the general notation, definitions and the appropriate linear models as well as other general information relating to repeated measures designs will be discussed. This is presented in the remainder of this chapter before moving onto construction of repeated measures designs which are 'best' for treatment and residual effects in Chapter 2.

1.2 Notation and Definitions

Firstly denote a repeated measures design (RMD) with t treatments, n experimental units, and p periods as RMD(t,n,p), and the class of all such designs as $\Omega_{t,n,p}$. A RMD can then be represented by a p x n array containing entries from {1,2,...,t}, called d, say, where d(i,j) represents the treatment assigned in the i^{th} period to the j^{th} unit. Then the *ordered pairs of treatment combinations* can be represented by (k,l), $1 \le k,l \le t$, where treatment k is applied to a given period and treatment l is applied in the following period for any given subject. Examples of RMDs(2,4,4) appear in Table 1.2-1.

A RMD is said to be *uniform on units* (or columns) if each treatment appears the same number of times in each column, and to be *uniform on periods* (or rows) if each treatment appears the same number of times in each row. A RMD is then said to be *uniform* if it is uniform on both columns and rows, each treatment appearing p/t times in each column and n/t times in each row. Design d_1 and d_3 in Table 1.2-1 are uniform RMDs, whereas design d_2 is uniform on neither rows nor columns.

d_1				d_2				d_3			
1	1	2	2	1	1	1	2	1	1	2	2
2	2	1	1	1	2	2	1	1	2	1	2
1	1	2	2	2	2	2	1	2	2	1	1
2	2	1	1	2	1	1	1	2	1	2	1

Table 1.2-1: *Examples of RMDs(2,4,4).*

If we let m_{ij} denote the number of times treatment j follows treatment i in design d, then we have the following definitions for RMDs.

Definition 1.2-1

A repeated measures design d is said to be *balanced* if

$m_{ij} = (1-\delta_{ij})\frac{n(p-1)}{t(t-1)}$, $1 \le i,j \le t$, $\forall$ i,j : i≠j, where δ_{ij} is the Kronecker δ and $m_{ii} = 0$. #

Definition 1.2-2

A repeated measures design d is said to be *strongly balanced* if

$$m_{ij} = \frac{n(p-1)}{t^2}, \quad 1 \le i,j \le t, \forall\ i,j. \qquad \#$$

That is, a RMD is said to be balanced if the number of times that each treatment follows all other treatments are equal and to be strongly balanced if the number of times each treatment follows all treatments (including itself) are equal.

A *strongly balanced, uniform RMD* (SBURMD) is then one which is both strongly balanced and uniform on both rows and columns, and similarly, a *balanced, uniform RMD* (BURMD) is one which is both balanced and uniform. Design d_1 in Table 1.2-1 is a BURMD with $m_{ij}=6$, design d_2 is a SBRMD and d_3 a SBURMD, both with $m_{ij}=3$. That is to say, for example, in d_3 the number of times all ordered pairs appear in the design is three.

A RMD is said to be *circular* if the last period in design d also precedes the first period. A circular RMD (CRMD) is also said to be strongly balanced, as in definition 1.2-2, if periods 0,1,...,p are considered where period 0 is the same as period p. Design d_3 in Table 1.2-1 has $m_{ij}=4$ if we consider it a CRMD. So Design d_3 is a SBURMD as well as a CSBURMD. It however, should be noted that not all CSBURMDs are also SBURMDs.

1.3 Linear Models

In all of the linear models that will be considered, it is assumed that there is only a first order residual treatment effect, that is, only a carry-over treatment effect from the previous

period. It is also assumed that all observations are independent of each other. These assumptions will be made for the remainder of this thesis. For a discussion on RMDs with observations on the same unit assumed to be correlated but observations between units independent see Street (1989). Matthews (1987) also discusses RMDs when two treatments are used and there are autocorrelated errors. It will also be assumed that the response variate measured will be continuous. For a discussion of RMDs when there is a binary response see Farewell (1985), and Kenward and Jones (1987).

If the RMDs are consider to be non-circular then the linear model

$$Y_{ij} = \mu + \alpha_i + \beta_j + \tau_{d(i,j)} + \rho_{d(i-1,j)} + E_{ij}, \qquad (1.3\text{-}1)$$

$$i = 1,2,...,p\ ,\ \ j = 1,2,...,n,\ \ \mathrm{Var}\,(E_{ij}) = \sigma^2,\ \ \rho_{d(0,j)} = 0,$$

can be used, where the constants μ, α, β, τ and ρ represent the general mean, the i^{th} period effect, the j^{th} unit effect, the direct treatment effect of d(i,j) and the residual (or carry-over) treatment effect from d(i-1,j), respectively, and Y_{ij} is the response measured on the i^{th} period and j^{th} unit. If the RMDs are considered circular then the linear model is the same except $\rho_{d(0,j)} = \rho_{d(p,j)}$. These linear models have been discussed by a number of authors (see, for example Cheng and Wu (1980), Kunert (1984) and Street (1989)). Hedayat and Afsarinejad (1978) and Hedayat (1981) have also discussed these models, with and without the inclusion of a period and/or subject effect.

Kok and Patterson (1976), Patterson (1970) and Sen and Mukerjee (1987) also considered a non-additive model, that is, the inclusion of an interaction term for direct and residual treatment effects. Let $\xi_{t_1t_2}$ $(1\le t_1,t_2\le t)$ represent the effect produced when treatment t_1 is applied in the current period and treatment t_2 is applied in the previous period. Then the linear model for the non-circular case is

$$Y_{ij} = \begin{cases} \mu + \alpha_i + \beta_j + \xi_{(d(i,j),d(i-1,j))} + E_{ij} & (2\le i\le p,\ 1\le j\le n) \\ \mu + \alpha_1 + \beta_j + \psi_{d(1,j)} + E_{1j} & (i=1,\ 1\le j\le n) \end{cases} \qquad (1.3\text{-}2)$$

where $\psi_{t_1} = \dfrac{\sum_{t_2=1}^{t} \xi_{t_1t_2}}{t}$ and $\mathrm{Var}\,(E_{ij}) = \sigma^2$. For the circular case the linear model is of the same form but does not have a ψ term for period 1, instead it has a ξ term using periods 1 and p.

1.4 Information Matrices for Estimating Direct and Residual Treatment Effects in RMDs

Consider the non-additive model (1.3-1), this can be written in the form $\mathbf{Y} = X\theta + \mathbf{E}$,

where $\theta = (\alpha_1,...,\alpha_p, \beta_1,...,\beta_n, \tau_1,...,\tau_t, \rho_1,...,\rho_t)^T$,

$\mathbf{Y} = (Y_{11}, Y_{21},..,Y_{p1},...,Y_{1n}, Y_{2n},..,Y_{pn})^T$,

$\mathbf{E} = (E_{11}, E_{21}, .., E_{p1}, ..., E_{1n}, E_{2n}, .., E_{pn})^T$,

and X is the *design matrix*, which is a (0,1) matrix. X^TX is then called the *information matrix* for estimating θ.

In RMDs the period and subject terms are usually included in the model but the emphasis is on estimating the direct and residual treatment effects. Hence $\mathbf{Y} = X\theta + \mathbf{E}$ can be partitioned into two components, that is

$$\mathbf{Y} = [X_1 \; X_2] \begin{bmatrix} \theta_1 \\ \theta_2 \end{bmatrix} + \mathbf{E},$$

where X_1 and θ_1 are for periods and subjects, and X_2 and θ_2 are for direct and residual treatments. The information matrix for estimation θ is then

$$X^TX = \begin{bmatrix} X_1^TX_1 & X_1^TX_2 \\ X_2^TX_1 & X_2^TX_2 \end{bmatrix},$$

and the information matrix for estimating direct treatment effects and residual treatment effects allowing for subject and period effects is

$$X_2^TX_2 - (X_2^TX_1)\,(X_1^TX_1)^-(X_1^TX_2),$$

where A^- denotes the generalized inverse of A. This can be further partitioned to give information matrices for direct and residual effects separately.

Street (1989) gave the explicit expressions for the information matrices for direct and residual treatment effects, which is presented below. This follows on from Hedayat and Afsarinejad (1978) and Cheng and Wu (1980). (The design d is considered non-circular but the following results also apply to circular design by considering periods 0,1,...,p instead of 1,2,...,p, where period 0 is the same as period p.)

For each design $d \in \Omega_{t,n,p}$, let

$N_u = (n_{iu})$ where n_{iu} is the number of times treatment i occurs on unit u,

$D = \text{diag}(r_1,..., r_t)$ where $r_i = \sum_u n_{iu}$,

$\tilde{N}_u = (\tilde{n}_{iu})$ where $\tilde{n}_{iu}$ is the number of times that treatment i occurs on unit u in the first p–1 periods,

$\tilde{D} = \text{diag}(\tilde{r}_1,..., \tilde{r}_t)$ where $\tilde{r}_i = \sum_u \tilde{n}_{iu}$,

$N_p = (h_{is})$ where h_{is} is the number of times that treatment i occurs in period s,

$\tilde{N}_p = (\tilde{h}_{is})$ where $\tilde{h}_{i1} = 0$, $\tilde{h}_{is} = h_{i,s-1}$, $s = 2,..., p$, and

$M = (m_{ij})$ where m_{ij} is the number of times that treatment i is preceded by treatment j.

The information matrix for estimating θ is $X^TX = \begin{bmatrix} D & M & N_p & N_u \\ M^T & \tilde{D} & \tilde{N}_p & \tilde{N}_u \\ N_p^T & \tilde{N}_p & nI_p & J_{p,n} \\ N_u^T & \tilde{N}_u & J_{n,p} & pI_n \end{bmatrix}$,

and information matrix for estimating direct treatment and residual treatment effects jointly is

$$\begin{bmatrix} C_{11} & C_{12} \\ C_{21} & C_{22} \end{bmatrix} = \begin{bmatrix} D & M \\ M^T & \tilde{D} \end{bmatrix} - \begin{bmatrix} N_p & N_u \\ \tilde{N}_p & \tilde{N}_u \end{bmatrix} \begin{bmatrix} nI_p & J_{p,n} \\ J_{n,p} & pI_n \end{bmatrix}^{-} \begin{bmatrix} N_p & N_u \\ \tilde{N}_p & \tilde{N}_u \end{bmatrix}^T,$$

where I_p is an identity matrix of size p and $J_{p,n}$ is a p x n matrix of ones.

The information matrix for estimating direct treatment effects is then

$$C_d = C_{11} - C_{12} C_{22}^{-} C_{21} \tag{1.4-1}$$

and the information matrix for estimating residual treatment effects is

$$C_r = C_{22} - C_{21} C_{11}^{-} C_{12}, \tag{1.4-2}$$

where

$$C_{11} = D - n^{-1} N_p N_p^T - p^{-1} N_u N_u^T + (np)^{-1} N_u J_{n,n} N_u^T, \tag{1.4-3}$$

$$C_{12} = C_{21}^T = M - n^{-1} N_p \tilde{N}_p^T - p^{-1} N_u \tilde{N}_u^T + (np)^{-1} N_u J_{n,n} \tilde{N}_u^T, \tag{1.4-4}$$

and $$C_{22} = \tilde{D} - n^{-1} \tilde{N}_p \tilde{N}_p^T - p^{-1} \tilde{N}_u \tilde{N}_u^T + (np)^{-1} \tilde{N}_u J_{n,n} \tilde{N}_u^T. \tag{1.4-5}$$

Example 1.4-1

Consider the following SBURMD(2,4,6) :

$$\begin{array}{cccc} 1 & 1 & 2 & 2 \\ 1 & 2 & 1 & 2 \\ 1 & 1 & 2 & 2 \\ 2 & 2 & 1 & 1 \\ 2 & 2 & 1 & 1 \\ 2 & 1 & 2 & 1 \end{array}$$

$$D = \begin{bmatrix} 12 & 0 \\ 0 & 12 \end{bmatrix},\ \tilde{D} = \begin{bmatrix} 10 & 0 \\ 0 & 10 \end{bmatrix},\ N_p = \begin{bmatrix} 2 & 2 & 2 & 2 & 2 & 2 \\ 2 & 2 & 2 & 2 & 2 & 2 \end{bmatrix},\ \tilde{N}_p = \begin{bmatrix} 0 & 2 & 2 & 2 & 2 & 2 \\ 0 & 2 & 2 & 2 & 2 & 2 \end{bmatrix},$$

$$M = \begin{bmatrix} 5 & 5 \\ 5 & 5 \end{bmatrix},\ N_u = \begin{bmatrix} 3 & 3 & 3 & 3 \\ 3 & 3 & 3 & 3 \end{bmatrix},\ \text{and}\ \tilde{N}_u = \begin{bmatrix} 3 & 2 & 3 & 2 \\ 2 & 3 & 2 & 3 \end{bmatrix}.$$

Hence $C_d = 6\begin{bmatrix} 1 & -1 \\ -1 & 1 \end{bmatrix}$ using (1.4-1) and $C_r = \frac{29}{6}\begin{bmatrix} 1 & -1 \\ -1 & 1 \end{bmatrix}$ using (1.4-2). #

A general MATLAB program to calculate C_d and C_r for a given design d appears in Appendix A.

1.5 Orthogonality of the Interaction Term in the Non-Additive Model

The non-additive model (1.3-2) can be written in the form $\mathbf{Y} = \mathbf{X}\theta + \mathbf{E}$, and can be partitioned for period and subject, and interaction, in a similar manner to the additive linear model (1.3-1) in Section 1.4. Sen and Mukerjee (1987) gave an explicit expression for the information matrix for estimation of the ξ's for circular, and non-circular, non-additive models. This is used to determine, for a given RMD(t,n,p), if direct treatment effects are orthogonal to both residual treatment effects and the direct by residual treatment interaction, and if residual effects are orthogonal to both direct treatment effects and the interaction.

Let e_i be a t x 1 vector with 1 in the i^{th} position and zero elsewhere,

1_t be a t x 1 vector of ones,

$J_t = 1_t 1_t'$,

$\lambda_{ij} = e_{d(i,j)} \otimes e_{d(i-1,j)}$, $(1 \le i \le p,\ 1 \le j \le n)$, for a circular model,

or

$$\lambda_{ij} = \begin{cases} e_{d(i,j)} \otimes e_{d(i-1,j)} & (2 \le i \le p,\ 1 \le j \le n), \\ t^{-1} e_{d(1,j)} \otimes 1_t & (i=1, 1 \le j \le n), \end{cases}$$ for a non-circular model,

$$M_d = (\sum_{i=1}^{p} \lambda_{i1}, \sum_{i=1}^{p} \lambda_{i2}, \ldots , \sum_{i=1}^{p} \lambda_{in}),$$

$$N_d = (\sum_{j=1}^{n} \lambda_{1j}, \sum_{j=1}^{n} \lambda_{2j}, \ldots , \sum_{j=1}^{n} \lambda_{pj}),$$

and

$$V_d = \sum_{i=1}^{p} \sum_{j=1}^{n} \lambda_{ij} \lambda_{ij}'.$$

Then the information matrix for estimating the ξ's in the non-additive model (1.3-2) is

$$C_d^* = V_d - n^{-1} N_d N_d^T - p^{-1} M_d M_d^T + (np)^{-1} (N_d 1_p) (N_d 1_p)^T. \qquad (1.5\text{-}1)$$

Now let $Z_1 = I_t \otimes J_t$ and $Z_2 = J_t \otimes I_t$. Then the following theorem can be used to determine orthogonality of the direct by residual treatment interaction and residual (direct) treatment effects with the direct (residual) treatment effects. The direct and residual effects are the main effects F_1 and F_2 respectively and their interaction is given by the interaction F_1F_2.

Theorem 1.5-1 (From Sen and Mukerjee (1987, Lemma 1.2))

In a design d, the best unbiased estimators of contrasts belonging to main effect F_1 (F_2) are orthogonal to those of contrasts belonging to main effect F_2 (F_1) and interaction F_1F_2 if and only if $Z_1C_d^*$ ($Z_2C_d^*$) is symmetric. #

A general MATLAB program to calculate $Z_1C_d^*$ and $Z_2C_d^*$ for a given RMD d appears in Appendix B. This is for a non-circular design; however, a similar program can be used for circular designs by using the appropriate λ_{ij}.

Chapter 2 Properties and Constructions of SBURMDs

This chapter discusses the 'best' type of repeated measures designs for the estimation of direct and residual treatment effects. These are SBURMDs and the justification appears in Section 2.1. The known constructions of SBURMDs are then presented in Section 2.2, as a basis for the rest of this thesis. Subsequently we construct all SBURMDs for given n, p, and small t, as there exist SBURMDs other than those currently given in the literature. In Section 2.3 we then discuss SBURMDs in terms of an example, and conclude with their merits.

2.1 Properties of SBURMDs

2.1.1 Optimality of SBURMDs

Kiefer (1975) introduced the concept of universal optimality as follows. Let $B_{t,0}$ be a collection of t x t non-negative definite matrices with zero row and column sums. Let Φ be a function such that Φ: $B_{t,0} \rightarrow (-\infty, \infty]$. A design with information matrix C is then said to be *universally optimal* if it is *Φ-optimal* for all Φ which satisfy:

(i) Φ is convex,

(ii) $\Phi(bC)$ is non-increasing in the scalar $b \geq 0$,

(iii) Φ is invariant under any simultaneous permutation of rows and columns of C.

Here a design is said to be *Φ-optimal for direct effects* if it minimises $\Phi(C_d)$ and to be *Φ-optimal for residual effects* if it minimises $\Phi(C_r)$ in a class of competing designs, where C_d and C_r are the information matrices for direct and residual treatment effects from Section 1.4. If a design is universally optimal, then it is D-,A-, and E-optimal (Kiefer (1975)).

Kiefer (1975) showed, equivalently, that a design is *universally optimal for a given effect* if the information matrix for this effect is symmetric, has maximum trace over all other designs in the class and the information matrix of every design in the class has zero row and column sums.

Cheng and Wu (1980, Lemma 2.1) proved that the row and column sums of C_d and C_r are zero for any $d \in \Omega_{t,n,p}$. Using this, and the concept of universal optimality, Cheng and Wu (1980) proved the following.

Theorem 2.1-1 (Cheng and Wu (1980, Theorem 3.1)

Let d^* be a strongly balanced uniform design in $\Omega_{t,n,p}$. Then d^* is universally optimal for the estimation of direct as well as residual effects over $\Omega_{t,n,p}$. #

Thus the information matrices for direct treatment effects (C_d) and residual treatment effects (C_r) are both symmetric, have maximum trace over all other designs $d \in \Omega_{t,n,p}$, and have row and column sums of zero. As an illustration of this the values of C_d and C_r are given for the three RMDs(2,4,4) in Example 2.2-1.

Example 2.1-1

For t=2, n=4, and p=4, consider the RMDs in Table 1.2-1. The Information matrices for direct and residual treatment effects are then as follows, where $C = \begin{bmatrix} 1 & -1 \\ -1 & 1 \end{bmatrix}$.

For d_1 (BRMD), $C_d = (0.7273)C$ and $C_r = (0.5)C$,

for d_2 (SBRMD), $C_d = (3.0556)C$ and $C_r = (2.2449)C$, and

for d_3 (SBURMD), $C_d = (4)C$ and $C_r = (2.75)C$. #

In fact, all SBURMDs for a given t, n and p have the same information matrices for direct and residual treatment effects. A general form of C_d and C_r can be obtained for SBURMDs(t,n,p) and is given below.

Theorem 2.1-2

For a SBURMD(t,n,p) the general form of C_d and C_r, both of size t x t, are

$$C_d = \frac{(t-1)np}{t^2} C, \text{ and } C_r = \frac{n(t-1)(p^2-p-1)}{t^2 p} C,$$

$$\text{where } C = \left(I_t + \frac{1}{t-1}(I_t - J_{t,t}) \right) = \begin{bmatrix} 1 & \frac{-1}{t-1} & \cdots & \frac{-1}{t-1} \\ \frac{-1}{t-1} & 1 & \cdots & \frac{-1}{t-1} \\ \cdot & \cdot & \cdot & \cdot \\ \frac{-1}{t-1} & \frac{-1}{t-1} & \cdots & 1 \end{bmatrix}.$$

#

The proof is given in Appendix C, using the results from Section 1.4.

2.1.2 Orthogonality of SBURMDs

2.1.2.a Additive Model

By definition SBURMDs and CSBURMDs have each pair of treatment combinations (including itself) appearing the same number of times in a design and hence direct and residual treatment effects are orthogonal.

2.1.2.b Non-Additive Model

Sen and Mukerjee (1987) proved that if the non-additive model (1.3-2) is considered then for a SBURMD d^* direct treatment effects are always orthogonal to residual treatment effects and the direct by residual interaction; see Theorem 2.1-3 below. However, it is not necessarily true that residual effects are orthogonal to direct effects and the interaction for the design d^*. That is to say, $Z_1C_d^*$ from Section 1.5 is always symmetric for a SBURMD but $Z_2C_d^*$ is not necessarily symmetric.

Theorem 2.1-4 is from Sen and Mukerjee (1987) and gives the conditions under which residual treatment effects are orthogonal to direct treatment effects and orthogonal to the direct by residual interaction for a SBURMD d^* (i.e. $Z_2C_d^*$ symmetric). The notation $S_d{}^*{}_h$ represents the set of units receiving treatment h ($1 \le h \le t$) in the last period, for any design $d^* \in \Omega_{t,n,p}$.

Theorem 2.1-3 (Sen and Mukerjee (1987, Theorem 3.1))

Under a non-additive model, d^* is universally optimal over $\Omega_{t,n,p}$ for the estimation of direct effects. #

Theorem 2.1-4 (Sen and Mukerjee (1987, Theorem 3.2))

Under a non-additive model, a SBURMD(t,n,p) d^* allows orthogonal estimation of the residual effects contrasts and hence becomes universally optimal over $\Omega_{t,n,p}$ for the residual effects if

(i) for each h,h' ($1 \le h,h' \le t$), there are exactly n/t^2 units receiving the treatments h and h' in the initial and the last periods respectively and

(ii) for each h ($1 \le h \le t$), in the collection of ordered pairs $\{d^*(i-1,j), d^*(i,j)\}$, $2 \le i \le p$, $j \in S_d{}^*_h$, each ordered pair (h,h_2) $(1 \le h_2 \le t)$ occurs the same number (say ν_1) of times while each ordered pair (h_1,h_2) $(1 \le h_1,h_2 \le t;\ h_1 \ne h)$ occurs the same number (say ν_2) of times. #

Sen and Mukerjee also reported that if condition (ii) above holds for d^* then for each treatment that appears in $S_d{}^*_h$

$$\nu_1 = \frac{n(p-t)}{t^3} \quad \text{and} \quad \nu_2 = \frac{np}{t^3}. \tag{2.1-1}$$

Example 2.1-2

Consider the following SBURMDs(2,4,6).

d_1:					d_2:				
	1	1	2	2		1	1	2	2
	1	2	1	2		1	2	1	2
	1	1	2	2		1	2	2	1
	2	2	1	1		2	2	1	1
	2	2	1	1		2	1	2	1
	2	1	2	1		2	1	1	2

i) All of the treatment combinations (1,1), (1,2), (2,1) or (2,2) representing the first and last period are present on each of $n/t^2=1$ units in both design d_1 and d_2.

ii) d_1: $S_d{}^*_1$ represents units 2 and 4 (which end with treatment 1), where each ordered pair (1,1) and (1,2) occurs 2 times (ν_1) while all other ordered pairs ((2,1) and (2,2)) occur 3 times (ν_2).

$S_d{}^*_2$ represents units 1 and 3, where the ordered pairs (2,1) and (2,2) occur 2 times (ν_1), and the ordered pairs (1,2) and (2,1) occur 3 times (ν_2).

d_2: $S_d{}^*_1$ represents units 2 and 3, however, the ordered pairs (1,1) and (1,2) do not appear ν_1 times on these units, and ordered pairs (2,1) and (2,2) do not appear ν_2 times. Similarly for $S_d{}^*_2$.

Hence design d_1 has the interaction term in the non-additive model (1.3-2) orthogonal to the direct and residual treatment effects, but design d_2 does not. This is the same as calculating $Z_1C_d^*$ and $Z_2C_d^*$ for both designs. Design d_1 has both $Z_1C_d^*$ and $Z_2C_d^*$ symmetric but in design d_2 $Z_2C_d^*$ is not symmetric. #

Kok and Patterson (1976) termed designs with direct treatment effects orthogonal to both the residual treatment effects and the interaction, and with the residual treatment effects orthogonal to both the direct treatment effects and the interaction, *R-orthogonal* . However, this was in relation to SBURMDs(t,t^2,2t) only, whereas the calculation of $Z_1C_d^*$ and $Z_2C_d^*$ apply for any SBURMD(t,n,p). The calculations which are used to define R-orthogonal designs appear in Appendix D but the calculations of $Z_1C_d^*$ and $Z_2C_d^*$ will be used here as this is a more general approach.

For CSBURMDs Kok and Patterson (1976) pointed out that for a design to be R-orthogonal, each ordered pair of treatments appears the same number of times within the sequences ending with a given value of t, where period 1 is regarded as subsequent to period p. So for example, considering the designs d_1 and d_2 in Example 2.1-1 the number of times each ordered pair appears in sequences ending with a 1 is the same as the number of times that they appear with the sequences ending with a 2. Hence if the designs d_1 and d_2 are considered circular then they are both R-orthogonal, that is $Z_1C_d^*$ and $Z_2C_d^*$ are symmetric in both designs.

2.2 Known Constructions of SBURMDs

SBURMDs are universally optimal for the estimation of direct treatment and residual treatment effects, as discussed in 2.1.1, and have direct effects orthogonal to residual treatment effects. Here we consider some designs which have appeared in the literature or which arise as general constructions of SBURMDs.

Cheng and Wu (1980, Theorem 3.2) proved that if $t^2|n$ and p/t is an *even* integer then there exists a SBURMD(t,n,p). Berenblut (1964), Patterson (1970) and Cheng and Wu (1980) give general constructions for SBURMDs(t,t^2,2t) and these appear in Section 2.2.2. Roy (1988) showed that SBURMDs exist when t|n and p/t is an *odd* integer provided $t \equiv 0,1,$ or 3(mod4), but that these designs may not exist for $t \equiv 2$(mod4). In particular SBURMDs(2,2,p) do not exist for *p* an odd multiple of 2. Sen and Mukerjee (1987) proved that there also exists a SBURMD(t,n,p) if $t^2|n$ and p/t is an *odd* integer. The general construction for this case

appears in Section 2.2.3. Other SBURMD(t,t^2,2t), constructed by Patterson (1973), for t=4, are discussed in Section 2.2.4.

2.2.1 Quenouille's SBURMDs

Quenouille (1953, pp.196-197) listed SBURMDs for t=2, t=3 and t=4. These are given in Tables 2.2-1 and 2.2-2. The design in Table 2.2-1 can be formed by taking all cyclical arrangements of the treatment sequence 1,1,2,2. Similarly using the sequences that appear in Table 2.2-2 and taking all possible cyclical arrangements of these, SBURMDs(3,18,6) and SBURMDs(4,16,8) are obtained.

Sequence	1	2	3	4
Period 1	1	1	2	2
2	1	2	2	1
3	2	2	1	1
4	2	1	1	2

Table 2.2-1: *Quenouille's SBURMD(2,4,4).*

Number of treatments	Use all cyclical arrangements of								
3	(a)						(b)		
	1	1	1				1	2	3
	1	1	2				1	2	3
	2	3	3				2	3	1
	2	3	2				3	1	2
	3	2	1				3	1	2
	3	2	3				2	3	1
4	(a)			(b)			(c)		
	1	1	1	1			1	3	
	1	3	1	3			1	3	
	2	2	2	3			2	1	
	2	1	2	2			3	4	
	3	4	3	4			4	2	
	3	2	4	1			4	2	
	4	4	4	4			3	4	
	4	3	3	2			2	1	

Table 2.2-2: *Quenouille's SBURMDs for t=3 and 4.*

Berenblut (1964) noted that the design in Table 2.2-1 has treatment 2 following treatment 1 as many times as treatment 1 does, and hence, that direct and residual treatment effects are orthogonal. This is, of course, true for all SBURMDs.

2.2.2 Construction of SBURMDs for t treatments, 2t periods and t^2 subjects

2.2.2.a Berenblut's Construction

Berenblut's (1964) construction for SBURMDs for the general case of t treatments, follows.

Let
$\alpha \equiv$ 1 2 3 4 ... t-1 t
$\beta \equiv$ t 1 2 3 ... t-2 t-1
$\gamma \equiv$ t-1 t 1 2 ... t-3 t-2
. . . . . .
$\psi \equiv$ 4 5 6 7 ... 2 3
$\phi \equiv$ 3 4 5 6 ... 1 2
$\omega \equiv$ 2 3 4 5 ... t 1

If t is odd then the design for t treatments is given in Table 2.2-3. If t is even then periods t and t+1, t-1 and t+2, etc., are interchanged.

Period	Subject 1 to t^2			
1	α	α	...	α
2	β	γ	...	α
3	γ	γ	...	γ
4	δ	ε	...	γ
.	.	.	...	.
t-1	ϕ	ω	...	ψ
t	ω	ω	...	ω
t+1	ω	α	...	ϕ
t+2	ϕ	ϕ	...	ϕ
.	.	.	...	.
2t-1	β	β	...	β
2t	α	β	...	ω

Table 2.2-3 : *Berenblut's general construction.*

So, for example, when t=2, $n=t^2=4$, and p=2t=4 then α = 1 2 and β = 2 1 and the design is (1) in Table 2.2-4. If t=3, n=9, and p=6, then α = 1 2 3, β = 3 1 2 and γ = 2 3 1, which gives (2), and similarly for t=4, n=16, and p=8 we get design (3) in Table 2.2-4.

(1) : SBURMD(2,4,4)

α	β	1	2	2	1
β	β	2	1	2	1
β	α	2	1	1	2
α	α	1	2	1	2

(2) : SBURMD(3,9,6)

α	α	α	1	2	3	1	2	3	1	2	3
β	γ	α	3	1	2	2	3	1	1	2	3
γ	γ	γ	2	3	1	2	3	1	2	3	1
γ	α	β	2	3	1	1	2	3	3	1	2
β	β	β	3	1	2	3	1	2	3	1	3
α	β	γ	1	2	3	3	1	2	2	3	1

(3) : SBURMD(4,16,8)

α	β	γ	δ	1	2	3	4	4	1	2	3	3	4	1	2	2	3	4	1
β	β	β	β	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3
γ	δ	α	β	3	4	1	2	2	3	4	1	1	2	3	4	4	1	2	3
δ	δ	δ	δ	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1
δ	α	β	γ	2	3	4	1	1	2	3	4	4	1	2	3	3	4	1	2
γ	γ	γ	γ	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2
β	γ	δ	α	4	1	2	3	3	4	1	2	2	3	4	1	1	2	3	4
α	α	α	α	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4

Table 2.2-4: *Examples of SBURMDs from Berenblut's construction.*

Design (1) is the same as the design given in Table 2.2-1 by Quenouille. If we compare the SBURMD(4,16,8) from Berenblut's (1964) method with Quenouille's three designs from Table 2.2-2, we see that the sequences of treatments which are applied to the subjects are not the same for any of the designs, that is they are *different* designs.

Berenblut states that interchanging even rows, odd rows and/or reading the constructed design in reverse, results in $2(t!)^2$ designs which are SBURMDs. In fact for t=2, by interchanging rows and reading in reverse we end up with the same design. For t=3, there are 72 possible designs. However, if all permutations of the treatment labels are considered, this results in only two non-isomorphic designs, that is design (2) in Table 2.2-4 and this design with rows 4 and 6 interchanged.

2.2.2.b Patterson's Construction

Patterson (1970) and Cheng and Wu (1980) also discussed SBURMDs$(t,t^2,2t)$. Their construction for these designs follows.

Consider periods 1 and 2 constructed such that they contain all of the ordered pairs of treatment combinations (k,l) , $1 \le k,l \le t$. Permute the treatments in periods 1 and 2, using the

permutation (123....t), to give periods 3 and 4 respectively. If $t \geq 3$, then permute the treatments in period 3 and 4, using the permutation (123...t), to give the treatments for periods 5 and 6. Continued until there are 2t periods. The resulting design is a SBURMD($t,t^2,2t$).

When t=2, the design produced by this method is the same as Quenouille's design given in Table 2.2-1. For t = 3 and 4 the designs produced appear as design (1) and (2) in Table 2.2-5. Design (1) in Table 2.2-5 and design (2) in Table 2.2-4 are different designs, in the sense that they do not have the same treatment sequences applied to the subjects, however, design (1) is design (2) from Table 2.2-4 with rows 4 and 6 interchanged as discussed by Berenblut (1964). Design (2) in Table 2.2-5 is also different to design (3) in Table 2.2-4 (which is different to the designs from Table 2.2-2).

(1): SBURMD(3,9,6)	(2): SBURMD(4,16,8)
1 1 1 2 2 2 3 3 3 1 2 3 1 2 3 1 2 3 2 2 2 3 3 3 1 1 1 2 3 1 2 3 1 2 3 1 3 3 3 1 1 1 2 2 2 3 1 2 3 1 2 3 1 2	1 1 1 1 2 2 2 2 3 3 3 3 4 4 4 4 1 2 3 4 1 2 3 4 1 2 3 4 1 2 3 4 2 2 2 2 3 3 3 3 4 4 4 4 1 1 1 1 2 3 4 1 2 3 4 1 2 3 4 1 2 3 4 1 3 3 3 3 4 4 4 4 1 1 1 1 2 2 2 2 3 4 1 2 3 4 1 2 3 4 1 2 3 4 1 2 4 4 4 4 1 1 1 1 2 2 2 2 3 3 3 3 4 1 2 3 4 1 2 3 4 1 2 3 4 1 2 3

Table 2.2-5 : *Kok and Patterson's SBURMDs for t=3 and t=4.*

Kok and Patterson (1976) called designs constructed in this manner *serial factorial designs* . These designs have the direct by residual treatment interaction effect orthogonal to direct treatment effects and residual treatment effects if the linear model is considered to be non-additive (equation (1.3-2)). That is, designs constructed in this way are R-orthogonal ($Z_1C_d^*$ and $Z_2C_d^*$ symmetric) as in Section 2.1.2.

2.2.3 Construction of SBURMDs for t treatments, p periods and t^2 subjects when p/t is an odd integer

Sen and Mukerjee (1987) proved the existence of SBURMDs when $n=t^2$ and p/t is an odd integer. They gave details of the construction of these designs using mutually orthogonal Latin squares.

The general construction for these designs follows. However, firstly recall that two Latin squares of the same order, say Q_1 and Q_2, are *orthogonal* if by superimposing one square on the other results in all possible ordered pairs appearing exactly once.

Sen and Mukerjee's Construction

(1) Let $pt^{-1} = 2m + 1$ $(m \geq 1)$, $t \neq 2,6$, and Q_1 and Q_2 be mutually orthogonal Latin squares with entries 0,1, ..., t–1 of order t.

(2) Let $G = (G_0, G_1, ..., G_{t-1})$,

where $G_i = (q_{1j}, q_{2j}, q_j)$, q_{ij} is the j^{th} column of Q_i and q_j is a t x 1 vector with all elements equal to j $(0 \leq j \leq t-1, i=1,2)$.

(3) If $m \geq 1$ then let $B = (B_0, B_1, ..., B_{t-1})$,

where $B_0 = \begin{bmatrix} 0 & 1 & \dots & t-1 \\ 0 & 0 & \dots & 0 \end{bmatrix}$ and $B_i = B_0 + [\, i \,](\mathrm{mod}(t))$.

(4) Let $A = (A_0', A_1', ..., A_{t-1}')$, where $A_0 = (G, B, ..., B)$, B appearing m-1 times and $A_i = A_0 + [\, i \,](\mathrm{mod}(t))$.

The p x t^2 array A is then a SBURMD(t, t^2, p). From this a SBURMD(t,n,p) satisfying the same conditions is obtained considering n/t copies of A.

For t = 2, use $G = \begin{bmatrix} 1 & 0 & 0 & 1 & 0 & 1 \\ 0 & 0 & 0 & 1 & 1 & 1 \end{bmatrix}$ and steps (3) and (4) above. #

The minimum requirement for these constructions are that $n = t^2$ and $p = 3t$ (m = 1) , in which case A is a 3t x t^2 array, where

$$A = [\, G_0' \quad G_1' \quad \dots \quad G_{t-1}' \,] = [\, G^* \,], \text{ say.}$$

When m = 2, p=3t+2t , the design is given by

$$A = \begin{bmatrix} G_0' & G_1' & \dots & G_{t-1}' \\ B_0' & B_1' & \dots & B_{t-1}' \end{bmatrix} = \begin{bmatrix} G^* \\ B^* \end{bmatrix}, \text{ say.}$$

The arrays G^* and B^* for t=2 and 3 are given in Tables 2.2-6 and 2.2-7 respectively, where the treatment labels are 1,2 (,3) instead of 0,1 (,2). Using these tables we can construct SBURMDs for t=2 or 3 for any p/t equal to any odd integer.

$G^* = (G_0'\ G_1')$	$B^* = (B_0'\ B_1')$
2 1 1 2 1 1 2 2 1 1 2 2 2 2 1 1 1 2 2 1 2 2 1 1	1 2 2 1 1 1 2 2 2 1 1 2 2 2 1 1

Table 2.2-6: *Design arrays for t=2 from Sen and Mukerjee.*

$G^* = (G_0'$	G_1'	$G_2')$	$B^* = (B_0'$	B_1'	$B_2')$
1 2 3	2 3 1	3 1 2	1 2 3	2 3 1	3 1 2
1 3 2	2 1 3	3 2 1	1 1 1	2 2 2	3 3 3
1 1 1	2 2 2	3 3 3	2 3 1	3 1 2	1 2 3
2 3 1	3 1 2	1 2 3	2 2 2	3 3 3	1 1 1
2 1 3	3 2 1	1 3 2	3 1 2	1 2 3	2 3 1
2 2 2	3 3 3	1 1 1	3 3 3	1 1 1	2 2 2
3 1 2	1 2 3	2 3 1			
3 2 1	1 3 2	2 1 3			
3 3 3	1 1 1	2 2 2			

Table 2.2-7: *Design arrays for t=3 from Sen and Mukerjee.*

2.2.4 Patterson's SBURMDs for t=4

Patterson (1973) showed that Quenouille's (1953) cyclic method of construction in Section 2.2.1 can be extended to construct any SBURMDs(t, t^2, 2t). Patterson in particular discussed RMDs when t=4, and pointed out that many designs other than the one constructed by Berenblut's (1964) method of Section 2.2.2.a (design (3) in Table 2.2-4) are also SBURMDs. Patterson found eight distinct SBURMDs(4,16,8). These eight designs can be obtained from the sequences in Table 2.2-8. For example, to obtain d_1, use the two sequences in the table and cycle through them to produce a SBURMD(4,16,8).

d_1	d_2	d_3	d_4	d_5	d_6	d_7	d_8
1 1	1 1	1 1	1 1	1 1	1 1	1 1	1 1
1 3	1 3	3 1	3 1	3 1	1 3	1 3	1 3
2 1	2 2	3 2	3 2	3 2	2 3	2 1	2 2
2 4	2 4	2 3	2 4	2 4	3 1	3 4	3 2
3 2	3 3	2 4	2 2	2 3	4 4	3 4	3 1
3 4	3 1	1 2	1 3	1 4	4 2	4 3	4 4
4 3	4 4	4 4	4 4	4 2	3 2	2 2	2 4
4 2	4 2	4 3	4 3	4 3	2 4	4 2	4 3

Table 2.2-8: *Patterson's SBURMDs for t=4.*

In general, Patterson (1973) gave a method of construction of SBURMDs for t an even integer, and the construction of *modified Quenouille's designs* for t an odd integer. For t=2 and 3 these produce designs that have been constructed via other methods. Since this thesis is concerned with small numbers of treatments, the methods of construction of these designs are not discussed here.

However, comparing the SBURMDs(4,16,18) of Sections 2.2.1 and 2.2.2 with the designs in Table 2.2-8, we can see the following. If the treatments in d_1 are permuted (4321) then this is the same as Quenouille's design (a) in Table 2.2-2, for t=4. Design d_6 is Quenouille's design (c) and design d_5 is Quenouille's design (b) when the permutation (13) is applied. Design d_2 is the same as the design (2) in Table 2.2-5 constructed by Patterson (1970). Hence the eight designs of Patterson (1973) are four previously known designs and four 'new' designs.

2.3 Comments on SBURMDs

SBURMDs have direct effects orthogonal to residual treatment effects, and they are universally optimal in the estimation of both these effects. Cheng and Wu (1980, Theorems 3.4, 3.5) also prove that they minimise the variance of linear unbiased estimators of any contrasts among the direct effects and the residual effects.

Hence they are 'best' in the estimation of direct, and of residual, treatment effects. So considering the example from Thornton *et al.*, (1987) where twelve subjects are used, two receiving each of the six sequences that appear in Table 1.1-1, it would have been better to give three subjects each of the four sequences in Table 2.2-1 to make up a SBURMD(2,12,4).

2.3.1 Orthogonality in the Non-additive Model for Constructed Designs

As an aside it should also be noted that all of the designs constructed in Section 2.2 have both direct and residual effects orthogonal to the direct by residual interaction (that is $Z_1C_d^*$ and $Z_2C_d^*$ symmetric (from Section 1.5)) when a non-additive model is considered. But not all SBURMDs have these properties, as discussed in Section 2.1.2.b.

2.3.2 SBURMDs as Building Blocks

SBURMDs exist when $t^2|n$ and p/t is either an even or odd integer. Given a SBURMDs$(t,t^2,2t)$ from Section 2.2, two such designs can be placed side-by-side to give a SBURMD$(t,2t^2,2t)$ or placed one under the other to give a SBURMD$(t,t^2,2(2t))$. SBURMDs$(t,2t^2,3t)$ can also be used in a similar way. Thus, in general, there are SBURMDs with $n=\lambda_1 t^2$ and $p=2\lambda_2 t$ or $p=3\lambda_2 t$ for all t, $\lambda_1 \geq 1$ and $\lambda_2 \geq 1$.

As an example, design (a) in Table 2.3-1 is the SBURMD(2,4,4) from Table 2.2-1, the designs (b) and (c) are also SBURMDs obtained from (a) by *horizontal* and *vertical pasting* respectively.

(a)	(b)	(c)
1 1 2 2	1 1 1 1 2 2 2 2	1 1 2 2
1 2 1 2	1 1 2 2 1 1 2 2	1 2 1 2
2 2 1 1	2 2 2 2 1 1 1 1	2 2 1 1
2 1 2 1	2 2 1 1 2 2 1 1	2 1 2 1
		1 1 2 2
		1 2 1 2
		2 2 1 1
		2 1 2 1

Table 2.3-1: *Examples of horizontal and vertical pasting.*

These are examples of pasting constructions. Such constructions ensure that once SBURMDs with the minimum values of n and p for a given t have been obtained, these can be used as 'building blocks' to construct SBURMDs for larger n and p for the same t. Pasting is investigated further in Chapters 3 and 4, where it can be used to construct non-isomorphic SBURMDs. However, prior to this, the construction of all SBURMDs with the minimum requirements of n and p for t=2 and 3 will be discussed.

Chapter 3 SBURMDs for Two Treatments

From Section 2.2, we have the existence of SBURMDs when $t^2|n$ and p/t is either an even or odd integer, and the known constructions for small values of t, n, and p were presented. When t=2, and p/t is an even integer, the smallest number of periods a SBURMD can have is four, and when p/t is an odd integer, the smallest number of periods is six. The SBURMDs for t=2 and p=4 and 6 are given in Tables 2.2-1 and 2.2-6 respectively.

From the definitions of Section 1.2, the necessary conditions for the existence of SBURMDs are t|p, t|n and $t^2|(p-1)n$. Hence, when t=2 and p=4, the necessary conditions are 2|4, 2|n and 4|3n. Thus the number of subjects for a SBURMD has to be a multiple of four, say n=4s, s≥1. When t=2, and p=6 the necessary conditions for a SBURMD again show that the number of subjects is a multiple of four.

Sections 3.1 and 3.2 are concerned with construction of SBURMDs when t=2, and p=4 and 6. Section 3.3 then looks at these designs for the non-additive model. These designs are then examined to determine whether some of these designs may be 'better' than others.

3.1 Construction for SBURMDs for t=2, n=4s and p=2t=4

Since SBURMDs are uniform on units (or columns), each column of the p x n array must contain two 1's and two 2's. Hence, each subject must receive one of six possible sequences. These sequences are listed in Table 3.1-1, where the sequences are denoted by S_i, i=1,2,...,6.

Sequence	S_1	S_2	S_3	S_4	S_5	S_6
Period 1	1	1	1	2	2	2
2	1	2	2	1	1	2
3	2	1	2	1	2	1
4	2	2	1	2	1	1

Table 3.1-1: *All sequences of length 4 containing two 1's and two 2's.*

For each sequence, the number of times the ordered pairs of treatments (1,1), (1,2), (2,1) and (2,2) appear on adjacent periods can then be considered. These appear in Table 3.1-2.

Sequence	S_1	S_2	S_3	S_4	S_5	S_6
$(1,1)^T$	1	0	0	1	0	1
$(1,2)^T$	1	2	1	1	1	0
$(2,1)^T$	0	1	1	1	2	1
$(2,2)^T$	1	0	1	0	0	1

Table 3.1-2:*The number of times the ordered pairs appear in each sequence.*

Now, let x_i , i=1, 2,...,6, be the number of units receiving treatment sequence S_i in a design. The x_i's must then sum to the total number of subjects in the design.

$$x_1 + x_2 + x_3 + x_4 + x_5 + x_6 = n = 4s \qquad (3.1\text{-}1)$$

The designs are also uniform on rows, and hence from Table 3.1-1 we get the following equations.

$$x_1 + x_2 + x_3 = n/t = n/2 = 2s \qquad (3.1\text{-}2a)$$

$$x_1 + x_4 + x_5 = 2s \qquad (3.1\text{-}2b)$$

$$x_2 + x_4 + x_6 = 2s \qquad (3.1\text{-}2c)$$

$$x_3 + x_5 + x_6 = 2s \qquad (3.1\text{-}2d)$$

Using Table 3.1-2 and the definition of strongly balanced, we then get the following equations.

$$x_1 + x_4 + x_6 = (p-1)n/t^2 = 3n/4 = 3s \qquad (3.1\text{-}3a)$$

$$x_1 + 2x_2 + x_3 + x_4 + x_5 = 3s \qquad (3.1\text{-}3b)$$

$$x_2 + x_3 + x_4 + 2x_5 + x_6 = 3s \qquad (3.1\text{-}3c)$$

$$x_1 + x_3 + x_6 = 3s \qquad (3.1\text{-}3d)$$

The above are then a system of linear equations of the form $A\mathbf{x}=\mathbf{b}$, where A is a 9 x 6 matrix of the coefficients of x_i's, and rank(A) = 5. Solving for $\mathbf{x}$ we obtain the following general solution using the particular solution $x_1= s$, $x_2= 0$, $x_3= s$, $x_4= s$, $x_5= 0$, $x_6= s$, and the kernel of A.

$$\mathbf{x} = \begin{bmatrix} x_1 \\ x_2 \\ x_3 \\ x_4 \\ x_5 \\ x_6 \end{bmatrix} = \begin{bmatrix} s+x_2 \\ x_2 \\ s-2x_2 \\ s-2x_2 \\ x_2 \\ s+x_2 \end{bmatrix}, \quad 0 \le x_2 \le \left[\frac{s}{2}\right], \quad s=1,2,3,\ldots,$$

where $\left[\frac{s}{2}\right]$ is the largest integer less than or equal to s/2. Since $x_1 = x_6$, $x_2 = x_5$, and $x_3 = x_4$, all of the designs have (1,2) as an automorphism. These results are then summarised in the following theorem.

Theorem 3.1-1

When t=2 and p=4, all strongly balanced, uniform repeated measures designs have n=4s units, s = 1, 2, ... There are $\left[\frac{s}{2}\right]+1$ non-isomorphic designs with 4s units and these designs have $a+s$ sequences of type S_1, and of type S_6, a sequences of type S_2, and of type S_5, and $s-2a$ sequences of type S_3 and S_4, where $a = 0, 1, 2, ..., \left[\frac{s}{2}\right]$. All of the designs have (1,2) as an automorphism. #

Hence, there is only one SBURMD(2,4,4) (a = 0 in Theorem 3.1-1), which is the SBURMD described by Quenouille (1953) and given in Table 2.2-1. For n=8, there are two SBURMDs (a = 0,1 in Theorem 3.1-1). The design corresponding to a =0 for n=8 can also be obtained by horizontally pasting the design for n=4, with the other design for n=8 (a = 1) being a 'new' design. The SBURMDs for n=4 and 8 appear in Table 3.1-3, where design d_1 for n=8 is obtained from design d_1 for n=4, and design d_2 for n=8 is a 'new' SBURMD.

n=4	n=8	
d_1	d_1	d_2
1 1 2 2	1 1 1 1 2 2 2 2	1 1 1 1 2 2 2 2
1 2 1 2	1 1 2 2 1 1 2 2	1 1 1 2 1 2 2 2
2 2 1 1	2 2 2 2 1 1 1 1	2 2 2 1 2 1 1 1
2 1 2 1	2 2 1 1 2 2 1 1	2 2 2 2 1 1 1 1

Table 3.1-3: *All SBURMDs for t=2, p=4 and n=4 and 8.*

In fact, all the designs with t=2 and p=4 are obtained by taking appropriate combinations of the design (x_1,x_2,x_3) = (1,0,1) when n=4 and the design (x_1,x_2,x_3) = (3,1,0) when n=8. This follows from Theorem 3.1-1, and is illustrated in Table 3.1-4 where all SBURMDs for n=12,16 and 20 are given.

n = 12	d_1	d_2
	1 1 1 1 1 1 2 2 2 2 2 2 1 1 1 2 2 2 1 1 1 2 2 2 2 2 2 2 2 2 1 1 1 1 1 1 2 2 2 1 1 1 2 2 2 1 1 1	1 1 1 1 1 1 2 2 2 2 2 2 1 1 1 1 2 2 1 1 2 2 2 2 2 2 2 2 1 2 1 2 1 1 1 1 2 2 2 2 2 1 2 1 1 1 1 1

n = 16		n = 20	
d_1	1 1 1 1 1 1 1 1 2 2 2 2 2 2 2 2 1 1 1 1 2 2 2 2 1 1 1 1 2 2 2 2 2 2 2 2 2 2 2 2 1 1 1 1 1 1 1 1 2 2 2 2 1 1 1 1 2 2 2 2 1 1 1 1	d_1	1 1 1 1 1 1 1 1 1 1 2 2 2 2 2 2 2 2 2 2 1 1 1 1 1 2 2 2 2 2 1 1 1 1 1 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 1 1 1 1 1 1 1 1 1 1 2 2 2 2 2 1 1 1 1 1 2 2 2 2 2 1 1 1 1 1
d_2	1 1 1 1 1 1 1 1 2 2 2 2 2 2 2 2 1 1 1 1 1 2 2 2 1 1 1 2 2 2 2 2 2 2 2 2 2 1 2 2 1 1 2 1 1 1 1 1 2 2 2 2 2 2 1 1 2 2 1 1 1 1 1 1	d_2	1 1 1 1 1 1 1 1 1 1 2 2 2 2 2 2 2 2 2 2 1 1 1 1 1 1 2 2 2 2 1 1 1 1 2 2 2 2 2 2 2 2 2 2 2 2 1 2 2 2 1 1 1 2 1 1 1 1 1 1 2 2 2 2 2 2 2 1 1 1 2 2 2 1 1 1 1 1 1 1
d_3	1 1 1 1 1 1 1 1 2 2 2 2 2 2 2 2 1 1 1 1 1 1 2 2 1 1 2 2 2 2 2 2 2 2 2 2 2 2 1 1 2 2 1 1 1 1 1 1 2 2 2 2 2 2 2 2 1 1 1 1 1 1 1 1	d_3	1 1 1 1 1 1 1 1 1 1 2 2 2 2 2 2 2 2 2 2 1 1 1 1 1 1 1 2 2 2 1 1 1 2 2 2 2 2 2 2 2 2 2 2 2 2 2 1 1 2 1 2 2 1 1 1 1 1 1 1 2 2 2 2 2 2 2 2 2 1 2 1 1 1 1 1 1 1 1 1

Table 3.1-4: *All SBURMDs for t=2, p=4 and n=12,16 and 20.*

3.2 Construction for SBURMDs for t=2, n=4s and p=3t=6

If we consider the case for p=6 in the same way as p=4 in Section 3.1, we can again obtain a set of linear equation to solve. There are now twenty possible sequences, each containing three 1's and three 2's. These are listed in Table 3.2-1.

Sequence	S_1	S_2	S_3	S_4	S_5	S_6	S_7	S_8	S_9	S_{10}	S_{11}	S_{12}	S_{13}	S_{14}	S_{15}	S_{16}	S_{17}	S_{18}	S_{19}	S_{20}
Period 1	1	1	1	1	1	1	1	1	1	1	2	2	2	2	2	2	2	2	2	2
2	1	1	1	1	2	2	2	2	2	2	1	1	1	1	1	1	2	2	2	2
3	1	2	2	2	1	1	2	1	2	2	1	1	2	1	2	2	1	1	1	2
4	2	1	2	2	1	2	1	2	1	2	1	2	1	2	1	2	1	1	2	1
5	2	2	1	2	2	1	1	2	2	1	2	1	1	2	2	1	1	2	1	1
6	2	2	2	1	2	2	2	1	1	1	2	2	2	1	1	1	2	1	1	1

Table 3.2-1: *All sequences of length 6 containing three 1's and three 2's.*

For each sequence, the number of times that the ordered pairs of treatments (1,1), (1,2), (2,1) and (2,2) appear on adjacent periods, are recorded in Table 3.2-2.

Sequence	S_1	S_2	S_3	S_4	S_5	S_6	S_7	S_8	S_9	S_{10}	S_{11}	S_{12}	S_{13}	S_{14}	S_{15}	S_{16}	S_{17}	S_{18}	S_{19}	S_{20}
$(1,1)^T$	2	1	1	1	1	0	1	0	0	1	2	1	1	1	0	1	2	1	1	2
$(1,2)^T$	1	2	2	1	2	3	2	2	2	1	1	2	2	1	2	1	1	1	1	0
$(2,1)^T$	0	1	1	1	1	2	1	2	2	1	1	2	2	2	3	2	1	2	2	1
$(2,2)^T$	2	1	1	2	1	0	1	1	1	2	1	0	0	1	0	1	1	1	1	2

Table 3.2-2: *The number of times the ordered pairs (1,1), (1,2), (2,1), (2,2) appear in each sequence.*

If x_i is now the number of units receiving treatment sequence S_i, i=1,2,...,20, in the design, then similar equations to those for p=4 can be set up, using the fact that the design is both strongly balanced and uniform on rows (periods). These equations appear in Appendix E.

These linear equations can again be expressed in the form $A\mathbf{x}=\mathbf{b}$, where A is a matrix of size 10 x 20, and rank(A) = 7. Solving these equations, we get the general solution

$$
\begin{aligned}
x_1 &= x_7 + x_9 + x_{10} + x_{13} + x_{15} + x_{16} + x_{17} + x_{18} + x_{19} + 2x_{20} - 2s,\\
x_2 &= x_7 + 2x_{10} - x_{15} + x_{16} + 2x_{17} + x_{18} + 2x_{19} + 3x_{20} - 3s,\\
x_3 &= -2x_7 + x_8 - 2x_{10} - x_{13} - x_{14} + x_{15} - x_{16} - 2x_{17} - x_{19} - 3x_{20} + 2s,\\
x_4 &= -x_8 - x_9 - x_{10} - x_{14} - x_{15} - x_{16} - x_{18} - x_{19} - x_{20} + 2s,\\
x_5 &= -2x_7 - x_9 - 2x_{10} + x_{12} + x_{14} + x_{15} - 2x_{17} - x_{18} - x_{19} - 3x_{20} + 3s,\\
x_6 &= x_7 - x_8 + x_{10} + x_{12} - x_{14} - x_{15} + x_{17} + 2x_{20} - s,\\
x_{11} &= -x_{12} - x_{13} - x_{14} - x_{15} - x_{16} - x_{17} - x_{18} - x_{19} - x_{20} + 2s,
\end{aligned}
$$

where $0 \le x_7, x_8, x_9, x_{10}, x_{12}, x_{13}, x_{14}, x_{15}, x_{16}, x_{17}, x_{18}, x_{19}, x_{20} \le 2s$, and $s = 1,2,3,\ldots$.

From the equivalent equations in Section 3.1 all SBURMDs can be found. Here all solutions to the above equations cannot be found very easily. When *s* is any integer value then the set of solutions to the above equations are a module which is finitely generated. The RMDs correspond to the positive elements of the module (De Launey (1989)). However, the basis of the module may only be expressible as linear combinations of the original x_i's. Hence this observation does not appear to make the task of finding the designs any easier.

However, for a SBURMD(2,4s,6), we need to choose $2s$ sequences from $S_1,S_2,...,S_{10}$, and $2s$ sequences from $S_{11},S_{12},...,S_{20}$, for uniformity on rows in the design. Using this fact, Pascal programs were set up to step through all possible combinations of **x** for a given n=4s. Then the x_i's that form solutions to $\mathbf{Ax}=\mathbf{b}$ are SBURMDs.

A Pascal program to find SBURMDs(2,4,6) appears in Appendix F, along with the solutions in terms of the x_i's. There are 15 non-isomorphic SBURMDs(2,4,6) and these appear in Table 3.2-3. Design d_2 in Table 3.2-3 is the same as the design constructed by Sen and Mukerjee (1987) in Section 2.2.3, which is the only design that has previously been constructed for t=2, n=4, p=6.

d_1	d_2	d_3	d_4	d_5	
1 1 2 2	1 1 2 2	1 1 2 2	1 1 2 2	1 1 2 2	symmetric designs
1 2 1 2	1 2 1 2	1 1 2 2	1 2 1 2	1 1 2 2	
1 1 2 2	1 2 1 2	2 2 1 1	2 2 1 1	2 2 1 1	
2 2 1 1	2 1 2 1	1 2 1 2	1 2 1 2	2 2 1 1	
2 2 1 1	2 2 1 1	2 2 1 1	2 1 2 1	1 2 1 2	
2 1 2 1	2 1 2 1	2 1 2 1	2 1 2 1	2 1 2 1	
d_6	d_7	d_8	d_9	d_{10}	
1 1 2 2	1 1 2 2	1 1 2 2	1 1 2 2	1 1 2 2	
1 2 1 2	1 2 1 2	1 2 1 2	2 2 1 1	2 2 1 1	
2 2 1 1	2 1 2 1	2 2 1 1	1 2 1 2	2 2 1 1	
2 2 1 1	2 1 2 1	2 1 2 1	1 2 1 2	1 2 1 2	
1 1 2 2	2 2 1 1	2 1 2 1	2 1 2 1	1 1 2 2	
2 1 2 1	1 2 1 2	1 2 1 2	2 1 2 1	2 1 2 1	
d_{11}	d_{12}	d_{13}	d_{14}	d_{15}	
1 1 2 2	1 1 2 2	1 1 2 2	1 1 2 2	1 1 2 2	non-symmetric designs
1 2 1 2	1 2 1 2	1 2 1 2	1 2 1 2	1 2 1 2	
1 2 2 1	1 2 2 1	1 2 2 1	1 2 2 1	2 2 1 1	
2 1 2 1	2 1 2 1	2 2 1 1	2 2 1 1	1 2 2 1	
2 1 1 2	2 2 1 1	2 1 1 2	2 1 2 1	2 1 2 1	
2 2 1 1	2 1 1 2	2 1 2 1	2 1 1 2	2 1 1 2	

Table 3.2-3: *All non-isomorphic SBURMDs(2,4,6).*

From these designs it can also be seen that it is not necessarily true that the designs have (1,2) as an automorphism, as is the case for p=4. Hence, designs can be classified as *symmetric* or *non-symmetric* as in Definition 3.2-1. Designs $d_1,d_2,...,d_{10}$ in Table 3.2-3 are then symmetric, and designs $d_{11},d_{12},...,d_{15}$ are non-symmetric.

Definition 3.2-1

A strongly balanced, uniform repeated measures design for t=2, n=4s, s=1,2,3,..., and p=6 is said to be *symmetric* if $x_1=x_{20}$, $x_2=x_{19}$, ... , and $x_{10}=x_{11}$, that is, it has (1,2) as an automorphism, otherwise the design is said to be *non-symmetric* . #

Using similar Pascal programs to the one that appears in Appendix F, it is also possible to find all SBURMDs for n=8,12,... . The total number of non-isomorphic (symmetric and non-symmetric) which result from these programs, for SBURMDs with t=2, p=6 and n=4,8, and 12 are given in Table 3.2-4.

n	4	8	12
symmetric	10	84	388
non-symmetric	5	130	1636
Total	15	214	2024

Table 3.2-4: *The number of non-isomorphic SBURMDs for t=2 and p=6.*

When t=2 and p=4, designs with n=4s, s≥3, are obtained by horizontally pasting an appropriate number of designs with n=4 and n=8, and they can be obtained in no other way. This is no longer the case when t=2 and p=6. Table 3.2-5 shows the number of designs for n=8 which can be obtained by horizontally pasting designs with n=4. Table 3.2-5 also gives the number of designs with n=12 which can be obtained by horizontally pasting designs with n=4 and/or n=8. (These were both calculated using Pascal programs, the program for the case when n=12 appears in Appendix G.) Hence, for p=6, pasting doesn't lead us to all designs. For n=8 there are 88 'new' designs which cannot be obtained from n=4 designs and for n=12, there are 150 'new' designs.

n	8	12
symmetric	51	380
non-symmetric	75	1494
Total	126	1874

Table 3.2-5: *The number of non-isomorphic SBURMDs possible using pasting for n=8 and 12.*

It should be noted that for n=4 the 10 symmetric designs, the 5 non-symmetric designs and the 5 non-symmetric designs permuted using (12) from Table 3.2-3 were considered for horizontal pasting for the designs for n=8 in Table 3.2-5. Similarly for the n=12 designs in Table 3.2-5 the 20 designs for n=4 and the 84 symmetric, 130 non-symmetric and 130 non-symmetric permuted using (12) were considered.

Non-symmetric designs permuted by (12) are included for pasting as they may lead to designs which cannot be obtained otherwise. Table 3.2-6 is a design for n=8 which is obtained by horizontally pasting the non-symmetric design d_{11} for n=4 from Table 3.2-3 and d_{11} with 1 and 2 interchanged. This design cannot be obtained by pasting any two designs in Table 3.2-3. For n=8 there are 12 such SBURMDs, two of which are symmetric.

1	1	2	2	2	2	1	1
1	2	1	2	2	1	2	1
1	2	2	1	2	1	1	2
2	1	2	1	1	2	1	2
2	1	1	2	1	2	2	1
2	2	1	1	1	1	2	2

Table 3.2-6: *An example of a SBURMD for t=2, p=6 and n=8 pasted from a non-symmetric design with the non-symmetric design permuted using (12).*

3.3 Using SBURMDs t=2, n=4s, and p=4 and 6 as Building Blocks

Having obtained all SBURMDs for t=2, n=4 and p=4 and 6, these can then be used to give SBURMDs for all t=2, n=4s and p= 8,10,12,... . By considering vertical and horizontal pasting as discussed in Section 2.3.2, any two SBURMDs with the same values of t and n, can always be pasted together vertically to produce a SBURMD for a larger value of p. This is summarised in the following Theorem.

Theorem 3.3-1

Let D_1 be a SBURMD(2,4s,p_1), and let D_2 be a SBURMD(2,4s,p_2), s= 1,2,... . Then there exists a SBURMD(2,4s,p_1+p_2). #

Proof

Let $D_3 = \begin{bmatrix} D_1 \\ D_2 \end{bmatrix}$, where the columns of D_1 are permuted such that the first n/2 columns have a 1 in the final row (and hence the remaining columns have a 2 in the final row), and the columns of D_2 are permuted such that the first n/4 columns begin with 1, the next n/4 columns begin with 2, the next n/4 columns begin with 1 and the final n/4 columns begin with 2. Then D_3 has t=2, $p=p_1+p_2$ and 4s units, and is uniform in rows and columns because D_1 and D_2 were. Using D_1, D_2, the method of construction of D_3, and Definition 1.2-2, we have

$$m_{ij} = \frac{n(p_1-1)}{4} + \frac{n(p_2-1)}{4} + \frac{n}{4} = \frac{n(p_1+p_2-1)}{4},$$

as required. Hence D_3 is a SBURMD(2,4s,p_1+p_2). #

Uniformity on the columns enables us to count s ordered pairs (1,1), (1,2), (2,1), (2,2) from the 'edges' of the two designs when they are vertically pasted, and since each design used is also strongly balanced the resulting design is also strongly balanced and uniform. This is illustrated by the designs in Table 3.3-1. Design (a) is a SBURMD(2,8,8) obtained by vertically pasting designs d_1 under design d_2 from Table 3.1-3, when n=8, once the columns have been permuted. Design (b) is a SBURMD(2,4,10), using design d_{11} from Table 3.2-3 and d_1 for n=4 from Table 3.1-3. Design (c) is a SBURMD(2,4,12), obtained from designs d_{10} and d_{15} from Table 3.2-3, once the columns of the design have been permuted.

(a)

2 2 2 2 1 1 1 1
1 2 2 2 1 1 1 2
2 1 1 1 2 2 2 1
1 1 1 1 2 2 2 2 } d_2

1 1 2 2 1 1 2 2
1 1 1 1 2 2 2 2
2 2 1 1 2 2 1 1
2 2 2 2 1 1 1 1 } d_1

(b)

2 2 1 1
1 2 1 2
2 1 1 2
2 1 2 1
1 2 2 1
1 1 2 2 } d_{11}

1 2 1 2
1 1 2 2
2 1 2 1
2 2 1 1 } d_1

(c)

1 2 1 2
2 1 2 1
2 1 2 1
2 2 1 1
1 2 1 2
1 1 2 2 } d_{10}

1 2 1 2
1 1 2 2
2 1 2 1
1 2 2 1
2 2 1 1
2 1 1 2 } d_{15}

Table 3.3-1: *Examples of SBURMDs obtained by vertical pasting.*

3.4 Discussion of Designs Constructed for t=2

From Section 2.1, SBURMDs for a given t, n, and p are 'best' in the estimation of direct and residual treatment effects. That is, the information matrices for both effects have maximum trace over all other RMDs(t,n,p). (For all RMDs the information matrices for both effects are completely symmetric (i.e., of the form aI+bJ) and have zero row and column sums. Thus using Kiefer's (1975) results, the design with maximum trace is universally optimal).

If we consider the additive model (1.3-1), and any SBURMDs(2,4s,p), p=4 or 6, s=1,2,..., constructed in Sections 3.1 and 3.2, then the information matrix for direct treatment effects (C_d) and the information matrix for residual effects (C_r) can be obtained from Theorem 2.1-2. The information matrices for any SBURMD(t,n,p) with p=4 and 6, n=4s, s=1,2, are given in Table 3.4-1.

t=2, n=4, p=4	t=2, n=8, p=4
$C_d = \begin{bmatrix} 4 & -4 \\ -4 & 4 \end{bmatrix}$ $C_r = \begin{bmatrix} 2.75 & -2.75 \\ -2.75 & 2.75 \end{bmatrix}$	$C_d = \begin{bmatrix} 8 & -8 \\ -8 & 8 \end{bmatrix}$ $C_r = \begin{bmatrix} 5.5 & -5.5 \\ -5.5 & 5.5 \end{bmatrix}$
t=2, n=4, p=6	t=2, n=8, p=6
$C_d = \begin{bmatrix} 6 & -6 \\ -6 & 6 \end{bmatrix}$ $C_r = \begin{bmatrix} 4.833 & -4.833 \\ -4.833 & 4.833 \end{bmatrix}$	$C_d = \begin{bmatrix} 12 & -12 \\ -12 & 12 \end{bmatrix}$ $C_r = \begin{bmatrix} 9.667 & -9.667 \\ -9.667 & 9.667 \end{bmatrix}$

Table 3.4-1: *Information matrices C_d and C_r for some SBURMDs.*

Although all SBURMDs for a given t, n, and p have universal optimality in the estimation of direct and residual treatment effects, some SBURMDs may be preferred to others if other criteria are used. The remainder of this chapter discusses this for some criteria, such as orthogonality, for the SBURMDs constructed in Sections 3.1 and 3.2, when t=2, n=4s, and p=4 or 6.

3.4.1 Orthogonality of SBURMDs with t=2

As discussed in Section 2.1.2.b, if the non-additive linear model (1.3-2) is assumed, then the residual treatment effects are not necessarily orthogonal to the direct treatment and direct by residual treatment interaction. However, even if it is assumed that there is no interaction term in the model, a SBURMD that has orthogonality of the interaction term is recommended as the direct treatment effects and residual treatment effects can then be estimated in exactly the same way as if there was no interaction.

3.4.1.a Orthogonality of SBURMDs(2,4s,4)

All of the SBURMDs in Table 3.1-3 (n=4 and 8) have the direct by residual interaction orthogonal. That is $Z_1C_d^*$ and $Z_2C_d^*$ from Section 1.5 are both symmetric, and the information matrices C_d^* associated with these designs (calculated using the Matlab program in Appendix B) are given in Table 3.4-2.

t=2, n=4, p=4 d_1	t=2, n=8, p=4 d_1	d_2
2.375 -0.375 -1.000 -1.000	4.75 -0.75 -2.00 -2.00	3.75 0.25 -1.00 -3.00
0.375 2.375 -1.000 -1.000	-0.75 4.75 -2.00 -2.00	0.25 3.75 -3.00 -1.00
1.000 -1.000 2.375 -0.375	-2.00 -2.00 4.75 -0.75	-1.00 -3.00 3.75 0.25
1.000 -1.000 -0.375 2.375	-2.00 -2.00 -0.75 4.75	-3.00 -1.00 0.25 3.75

Table 3.4-2: *Information matrix C_d^* for the SBURMDs in Table 3.1-3.*

It should be noted that all of these designs have (1,2) as an automorphism, and as such are symmetric designs by Definition 3.2-1. Hence, if we consider Theorem 2.1-2, once all sequences in a design ending with a 1 are looked at, we automatically have the compliment in the sequences ending with a 2, so that ν_1 and ν_2 are of the form of equation (2.1-1). Because of the conditions of strongly balanced and uniformity, a symmetric design, for t=2, will then always comply with this counting method and as such have residual treatment effects orthogonal to the interaction.

Since all SBURMDs(2,4s,4) can be constructed from the n=4 and 8 designs, and are also symmetric, they all have orthogonality of the interaction term with the residual treatment effects as well as with the direct treatment effects.

3.4.1.b Orthogonality of SBURMDs(2,4s,6)

Sen and Mukerjee (1987) noted that not all SBURMDs have residual treatment effects which are orthogonal to the direct treatment effects and to the direct by residual treatment interaction. If we consider the fifteen SBURMDs from Table 3.2-3, and calculate $Z_1C_d^*$ and $Z_2C_d^*$ using the Matlab program in Appendix B, we find that all of the symmetric SBURMDs $(d_1,d_2,...,d_{10})$ have residual treatment effects orthogonal to direct treatment effects and to the direct by residual treatment interaction, as do the non-symmetric designs d_{13} and d_{15}. However, designs d_{11}, d_{12}, and d_{14} do not have residual treatment effects orthogonal to both the direct treatment effects and the direct by residual treatment interaction. C_d^*, $Z_1C_d^*$ and $Z_2C_d^*$ for the fifteen SBURMDs(2,4,6) appear in Appendix H.

3.4.2 Families of Designs

Consider the fifteen SBURMDs(2,4,6) in Table 3.2-3. If design d_1 was selected for use in a RMD experiment, and say, something went wrong in period 1, then by repeating period 1 after period 6 in d_1, and ignoring the original period 1, we have the SBURMD d_7. We will call this *cycling the design by one period.* Cycling d_7, we have the SBURMD d_{10}. However, not all SBURMDs(2,4,6) result in another SBURMD when the design is cycled by one period. As an example, when d_{10} is cycled by one period the resulting design is not a SBURMD, but it is strongly balanced and uniform if we consider the design to be circular (CSBURMD). An illustration of this appears in Table 3.4-3, using design d_1 and cycling through one period at a time.

d_1					
1 1 2 2	1 2 1 2	1 1 2 2	2 2 1 1	2 2 1 1	2 1 2 1
1 2 1 2	1 1 2 2	2 2 1 1	2 2 1 1	2 1 2 1	1 1 2 2
1 1 2 2	2 2 1 1	2 2 1 1	2 1 2 1	1 1 2 2	1 2 1 2
2 2 1 1	2 2 1 1	2 1 2 1	1 1 2 2	1 2 1 2	1 1 2 2
2 2 1 1	2 1 2 1	1 1 2 2	1 2 1 2	1 1 2 2	2 2 1 1
2 1 2 1	1 1 2 2	1 2 1 2	1 1 2 2	2 2 1 1	2 2 1 1
	↓	↓	↓	↓	↓
	d_7	d_{11}	NOT SBURMD	NOT SBURMD	d_4

Table 3.4-3: *Cycling through d_1, one period at a time.*

All of the SBURMDs(2,4,6) can be considered in this way. We find that there are three *families* of symmetric designs and three *families* of non-symmetric designs. This is illustrated in Table 3.4-4, where $d_{i'}$ represent designs d_i , i = 11,12,...,15, when permuted using (1,2). It should be noted that if we consider CRMDs(2,4,6) (so period 6 precedes period 1, as discussed in Section 1.2), then all SBURMDS(2,4,6) from Table 3.2-3 are also CSBURMDs(2,4,6), with the exception of design d_{11} which is no longer strongly balanced. However, when we cycle through the design one period at a time, the designs that are not SBURMDs are all CSBURMDs, again with the exception of design d_{11}. In fact, if we set up a similar Pascal program to the one in Appendix F to find all CSBURMDs(2,4,6), we find that they can all be obtained by cycling through the SBURMDs(2,4,6) that are also CSBURMDs(2,4,6).

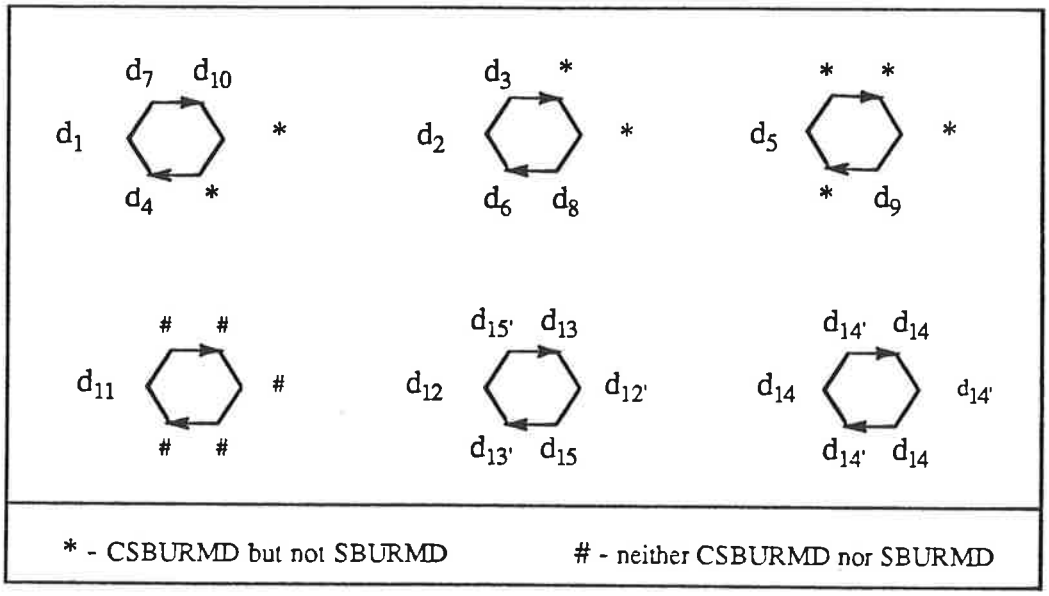

Table 3.4-4: *Families of designs belonging to SBURMDs(2,4,6).*

3.4.3 Conclusions about SBURMDs with t=2

From Section 3.4.1 and 3.4.2, we now have some further information for the selection of a SBURMD. When t=2, n=4s, and p=4, all of the SBURMDs have the interaction of the direct and residual treatment effects orthogonal to the residual treatment effects and to the direct treatment effects. On this basis, any of the SBURMDs could be selected. However, this is not true for t=2, n=4, p=6, where three of the SBURMDs (d_{11}, d_{12} and d_{14}) do not have

orthogonality of the interaction term. If SBURMDs(2,4s,6) are to be constructed from horizontal pasting of SBURMDs(2,4,6), by considering any of the designs $d_1,\ldots,d_{10},d_{13},d_{15}$, orthogonality of the interaction term is automatically guaranteed. From Table 3.4-4, we can further conclude that designs d_4 and d_8 would be best if the effects of the first period are likely to be lost, or otherwise measured incorrectly.

Chapter 4 SBURMDs for Three and Four Treatments

When the method of construction for the SBURMDs from Section 3.1 and 3.2 is considered for three or more treatments, the situation becomes more complicated. In Sections 4.1 and 4.2 this is illustrated by considering the construction of SBURMDs for t=3 and p=6. Based upon this discussion, SBURMDs for t=4 are briefly discussed in Section 4.3, only in relation to those designs already constructed, with a follow-up discussion on SBURMDs with a 2 x 2 factorial treatment structure applied.

4.1 Construction for SBURMDs for t=3, n=9s and p=2t=6

When t=3, and p/t is an even integer, the smallest number of periods a SBURMD can have is six. From the definitions of Section 1.2, the necessary conditions for the existence of SBURMDs are t|p, t|n and t^2|(p-1)n. Hence, when t=3 and p=6, the necessary conditions are 3|6, 3|n and 9|5n. Thus the number of subjects for a SBURMD has to be a multiple of nine, say n=9s, s≥1.

From the literature, there are two SBURMDs(3,6,9), which are given as design (2) in Table 2.2-4 (Berenblut's 1964 construction) and design (1) in Table 2.2-5 (Patterson's 1970 construction). For SBURMDs(2,6,18) there are two designs, given by Quenouille (1953), which appear in Table 2.2-2.

If we consider the construction of SBURMDs with t=2 and p=6 in a similar way to Sections 3.1 and 3.2, we find that there are now 90 sequences of length 6 which contain two 1's, two 2's and two 3's. As observed in Pattison and Street (1989) , these can be grouped into 15 sets of 6 sequences each, where sequences in a set can be obtained from each other by applying a permutation of 1,2 and 3 (that is, an element of the permutation group S_3). The 90 sequences, grouped into 15 sets of 6, appear in Table 4.1-1, and are denoted $S_{i,j}$, i=1,2,...,15, and j=1,2,...,6.

From these 90 sequences we can consider the number of times the ordered pairs of treatments (1,1), (1,2), (1,3), (2,1), (2,2), (2,3), (3,1), (3,2) and (3,3) appear on adjacent periods for each sequence, in a similar manner to Section 3.1. If we let x_k, k=1,2,3,...,90, be

	Period 1 2 3 4 5 6		k	Period 1 2 3 4 5 6		k	Period 1 2 3 4 5 6		k
	1 1 2 2 3 3	$s_{1,1}$	1	1 1 2 3 2 3	$s_{2,1}$	7	1 1 2 3 3 2	$s_{3,1}$	13
(123)	2 2 3 3 1 1	$s_{1,2}$	2	2 2 3 1 3 1	$s_{2,2}$	8	2 2 3 1 1 3	$s_{3,2}$	14
(132)	3 3 1 1 2 2	$s_{1,3}$	3	3 3 1 2 1 2	$s_{2,3}$	9	3 3 1 2 2 1	$s_{3,3}$	15
(23)	1 1 3 3 2 2	$s_{1,4}$	4	1 1 3 2 3 2	$s_{2,4}$	10	1 1 3 2 2 3	$s_{3,4}$	16
(12)	2 2 1 1 3 3	$s_{1,5}$	5	2 2 1 3 1 3	$s_{2,5}$	11	2 2 1 3 3 1	$s_{3,5}$	17
(13)	3 3 2 2 1 1	$s_{1,6}$	6	3 3 2 1 2 1	$s_{2,6}$	12	3 3 2 1 1 2	$s_{3,6}$	18
	1 2 1 2 3 3	$s_{4,1}$	19	1 2 1 3 2 3	$s_{5,1}$	25	1 2 1 3 3 2	$s_{6,1}$	31
(123)	2 3 2 3 1 1	$s_{4,2}$	20	2 3 2 1 3 1	$s_{5,2}$	26	2 3 2 1 1 3	$s_{6,2}$	32
(132)	3 1 3 1 2 2	$s_{4,3}$	21	3 1 3 2 1 2	$s_{5,3}$	27	3 1 3 2 2 1	$s_{6,3}$	33
(23)	1 3 1 3 2 2	$s_{4,4}$	22	1 3 1 2 3 2	$s_{5,4}$	28	1 3 1 2 2 3	$s_{6,4}$	34
(12)	2 1 2 1 3 3	$s_{4,5}$	23	2 1 2 3 1 3	$s_{5,5}$	29	2 1 2 3 3 1	$s_{6,5}$	35
(13)	3 2 3 2 1 1	$s_{4,6}$	24	3 2 3 1 2 1	$s_{5,6}$	30	3 2 3 1 1 2	$s_{6,6}$	36
	1 2 2 1 3 3	$s_{7,1}$	37	1 2 3 1 2 3	$s_{8,1}$	43	1 2 3 1 3 2	$s_{9,1}$	49
(123)	2 3 3 2 1 1	$s_{7,2}$	38	2 3 1 2 3 1	$s_{8,2}$	44	2 3 1 2 1 3	$s_{9,2}$	50
(132)	3 1 1 3 2 2	$s_{7,3}$	39	3 1 2 3 1 2	$s_{8,3}$	45	3 1 2 3 2 1	$s_{9,3}$	51
(23)	1 3 3 1 2 2	$s_{7,4}$	40	1 3 2 1 3 2	$s_{8,4}$	46	1 3 2 1 2 3	$s_{9,4}$	52
(12)	2 1 1 2 3 3	$s_{7,5}$	41	2 1 3 2 1 3	$s_{8,5}$	47	2 1 3 2 3 1	$s_{9,5}$	53
(13)	3 2 2 3 1 1	$s_{7,6}$	42	3 2 1 3 2 1	$s_{8,6}$	48	3 2 1 3 1 2	$s_{9,6}$	54
	1 2 2 3 1 3	$s_{10,1}$	55	1 2 3 2 1 3	$s_{11,1}$	61	1 3 2 2 1 3	$s_{12,1}$	67
(123)	2 3 3 1 2 1	$s_{10,2}$	56	2 3 1 3 2 1	$s_{11,2}$	62	2 1 3 3 2 1	$s_{12,2}$	68
(132)	3 1 1 2 3 2	$s_{10,3}$	57	3 1 2 1 3 2	$s_{11,3}$	63	3 2 1 1 3 2	$s_{12,3}$	69
(23)	1 3 3 2 1 2	$s_{10,4}$	58	1 3 2 3 1 2	$s_{11,4}$	64	1 2 3 3 1 2	$s_{12,4}$	70
(12)	2 1 1 3 2 3	$s_{10,5}$	59	2 1 3 1 2 3	$s_{11,5}$	65	2 3 1 1 2 3	$s_{12,5}$	71
(13)	3 2 2 1 3 1	$s_{10,6}$	60	3 2 1 2 3 1	$s_{11,6}$	66	3 1 2 2 3 1	$s_{12,6}$	72
	1 2 2 3 3 1	$s_{13,1}$	73	1 2 3 2 3 1	$s_{14,1}$	79	1 2 3 3 2 1	$s_{15,1}$	85
(123)	2 3 3 1 1 2	$s_{13,2}$	74	2 3 1 3 1 2	$s_{14,2}$	80	2 3 1 1 3 2	$s_{15,2}$	86
(132)	3 1 1 2 2 3	$s_{13,3}$	75	3 1 2 1 2 3	$s_{14,3}$	81	3 1 2 2 1 3	$s_{15,3}$	87
(23)	1 3 3 2 2 1	$s_{13,4}$	76	1 3 2 3 2 1	$s_{14,4}$	82	1 3 2 2 3 1	$s_{15,4}$	88
(12)	2 1 1 3 3 2	$s_{13,5}$	77	2 1 3 1 3 2	$s_{14,5}$	83	2 1 3 3 1 2	$s_{15,5}$	89
(13)	3 2 2 1 1 3	$s_{13,6}$	78	3 2 1 2 1 3	$s_{14,6}$	84	3 2 1 1 2 3	$s_{15,6}$	90

Table 4.1-1: *90 possible sequences for t=3 and p=6.*

the number of units receiving treatment sequence $S_{i,j}$ in the final design, (see Table 4.1-1 for the appropriate subscripts), and we consider the ordered pairs of treatments, we can again set up a system of linear equations of the form **Ax=b**. The uniformity in rows gives us 3x6 = 18 equations and the strongly balanced property gives us a further 9 equations. However, the equations are not independent (for instance as there can only be 1's, 2's and 3's in each row, once the number of 1's and 2's are known, the number of 3's is also). In fact, rank(A) = 15. The system of linear equations, where A is of full row rank is given in Appendix I. A general solution for **x** can then be found using the particular solution associated with design (1) in Table 2.2-5, and the Kernel of A, and is also given in Appendix I. From this general solution, there are 15 variables which depend on the selection of the other 75. This does not make the task of finding the solutions for SBURMDs(2,9s,6) any easier.

In Section 3.2, the solutions for all SBURMDs(2,4,6) were found using a Pascal program which looped over all possible combinations of x_i's such that **Ax=b**, ($\binom{10}{2}^2 = 2025$ combinations) . However, for t=3, n=9 and p=6 there are $\binom{30}{3}^3 \approx 6.69 \times 10^{10}$ possible combinations of x_i's. Hence, a simplified method to find at least some of the SBURMDs for t=3 is required. This is discussed in the following section.

4.1.1 Symmetric and Partially-Symmetric SBURMDs with t=3

In Section 3.2, designs were defined as being either symmetric or non-symmetric for SBURMDs(2,4s,6) in Definition 3.2-1. In a similar manner we can define symmetric SBURMDs for t=3 , n=18,36,54,..., and p=6 as follows.

Definition 4.1-1

A strongly balanced, uniform, repeated measures design for t=3, n=9s, s=2,4,6,..., and p=6 is said to be *symmetric* if the permutations (123), (132), (23), (12) and (13) of a sequence in the design are also in the strongly balanced, uniform repeated measures design. (That is those designs for which all the elements of S_3 are an automorphism.) #

As an example, when n=18, the SBURMD which contains the sequences $S_{1,1}$, ..., $S_{1,6}$, $S_{2,1}$, ..., $S_{2,6}$, $S_{4,1}$, ..., $S_{4,6}$ is a symmetric SBURMD(3,18,6).

For n=9, 27, 45,..., these symmetric designs do not exist. However, if we consider the sequences $S_{1,j}$, j = 1,2,3,..,6, these can be split into two groups, where sequences $S_{1,1}$ and $S_{1,4}$ can both be permuted by (123) and (132) to give the six sequences, where the two groups are related by the permutation (23). Hence the 15 sets of 6 sequences can be considered as 15 sets of 3 sequences and the 15 sets of 3 sequences permuted (23). *Partially-symmetric* SBURMDs for t=3 can then be defined as follows.

Definition 4.1-2

A strongly balanced, uniform repeated measures design is known as *partially-symmetric* if a given sequence and the sequences permuted using (123) and (132) also appear in the design. #

The two SBURMDS(3,9,6) constructed by Berenblut (1964) and Patterson (1970) are then both partially-symmetric. Patterson's design consists of sequences $S_{1,1}$, $S_{1,2}$, $S_{1,3}$, $S_{8,4}$, $S_{8,5}$, $S_{8,6}$, $S_{13,1}$, $S_{13,2}$, and $S_{13,3}$. Berenblut's designs consists of $S_{3,1}$, $S_{3,2}$, $S_{3,3}$, $S_{7,1}$, $S_{7,2}$, $S_{7,3}$, $S_{15,4}$, $S_{15,5}$, and $S_{15,6}$.

To find the partially-symmetric SBURMDs, let px_i , i=1,2,3,...30, be the number of times sequences of the type $S_{i,j}$, i=1,2,3,...15, j=1,4, appear in a SBURMD. Then, using the method of Sections 3.1 and 3.2, a set of linear equations can be obtained, where rank(A)=3. The linear equations based on the number of times the ordered pairs (1,2), (1,3) and (2,2) occur in the three sequences has full row rank, and appears as Equation (4.1-1).

$$\begin{bmatrix} 2&0&3&1&2&1&3&1&2&3&1&3&1&2&5&0&3&2&3&1&2&3&0&4&3&0&4&1&2&2 \\ 0&2&1&3&1&2&1&3&3&2&3&1&2&1&0&5&2&3&1&3&3&2&4&0&0&3&1&4&2&2 \\ 3&3&1&1&2&2&1&1&0&0&1&1&2&2&0&0&0&0&1&1&0&0&1&1&2&2&0&0&1&1 \end{bmatrix} \begin{bmatrix} px_1 \\ px_2 \\ .. \\ px_{30} \end{bmatrix} = \begin{bmatrix} 5s \\ 5s \\ 5s \end{bmatrix} \qquad (4.1\text{-}1)$$

Using the above linear equations and the Pascal programs in Appendix J, there are 51 non-isomorphic SBURMDs(3,9,6) that are partially-symmetric. These 51 designs appear in Appendix K, and they can then be used as 'building blocks' for larger SBURMDs with t=3.

For n=18 (s=2), 4471 SBURMDs can be found in the same way. Pattison and Street

(1989) considered those designs for which all the elements of S_3 are an automorphism, and showed that there are 72 symmetric SBURMDs(3,18,6). The appropriate linear equations are given here as Equation (4.1-2), where sx_i represents the number of sequences of type $S_{i,1}$, i=1,2,3,...,15, and hence the number of times the other 5 sequences in the permutation group are present. There are two independent equations that the 15 unknowns must satisfy, which are based on the number of times the ordered pairs (1,1) and (1,2) occur in the group of six sequences for all $S_{i,1}$. The solutions appear in Appendix L.

$$\begin{bmatrix} 6 & 2 & 4 & 2 & 0 & 2 & 4 & 0 & 0 & 2 & 0 & 2 & 4 & 0 & 2 \\ 2 & 4 & 3 & 4 & 5 & 4 & 3 & 5 & 5 & 4 & 5 & 4 & 3 & 5 & 4 \end{bmatrix} \begin{bmatrix} sx_1 \\ sx_2 \\ .. \\ sx_{15} \end{bmatrix} = \begin{bmatrix} 5s \\ 5s \end{bmatrix} \qquad (4.1\text{-}2)$$

The following Table gives the number of SBURMDS(3,9s,6), that have been found for partially-symmetric and symmetric designs for s=1,2. It should be noted, however, that these are not the only SBURMDs that exist for t=3, n=9,18, but they represent the SBURMDs which can be found most readily.

	n = 9	n =18
Total Number of Partially-Symmetric Designs	51	4471
Partially-Symmetric Designs that are also Symmetric	-	72
Partially-Symmetric Only	51	4399

Table 4.1-2: *Number of symmetric and partially-symmetric, non-isomorphic SBURMDs for t=3, n=9,18 and p=6.*

4.2 Information Matrices for t=3, n=9s and p=2t=6

4.2.1 Additive Model

Table 4.2-1 contains the information matrices for direct treatment effects and residual treatment effects for any SBURMD(3,9s,6), s=1,2, with the additive linear model (1.3-1), calculated from Theorem 2.1.2.

t=3, n=9, p=6	t=3, n=18, p=6
$C_d = \begin{bmatrix} 12 & -6 & -6 \\ -6 & 12 & -6 \\ -6 & -6 & 12 \end{bmatrix}$	$C_d = \begin{bmatrix} 18 & -9 & -9 \\ -9 & 18 & -9 \\ -9 & -9 & 18 \end{bmatrix}$
$C_r = \begin{bmatrix} 9.667 & -4.833 & -4.833 \\ -4.833 & 9.667 & -4.833 \\ -4.833 & -4.833 & 9.667 \end{bmatrix}$	$C_r = \begin{bmatrix} 15.778 & -7.889 & -7.889 \\ -7.889 & 15.778 & -7.889 \\ -7.889 & -7.889 & 15.778 \end{bmatrix}$

Table 4.2-1: *Information matrices C_d and C_r for SBURMDs(3,9s,6), s=1,2.*

4.2.2 Non-Additive Model

If we consider the linear model to be non-additive, we can again show that some of the SBURMDs have the direct by residual treatment interaction orthogonal to the direct treatment effects and the residual treatment effects. The matrices $Z_1C_d^*$ and $Z_2C_d^*$ from Section 1.5 can be calculated using the Matlab program in Appendix B.

If we consider the 51 partially-symmetric SBURMDs(3,9,6) in Appendix K, there are 13 designs that have both $Z_1C_d^*$ and $Z_2C_d^*$ symmetric, indicating the orthogonality of the interaction term. These 13 designs are identified in Appendix K. If we consider Theorem 2.1-4, this says that the number of times that each ordered pair appears in the sequences ending with treatment t, t=1,2,3, are as indicated in Table 4.2-2, where $\nu_1 = 1$ and $\nu_2 = 2$. It should be noted, that the two SBURMDs(3,9,6) previously constructed are included amongst these 13 designs.

ordered pairs	Sequences ending in 1	2	3
$\binom{1}{1}$	1	2	2
$\binom{1}{2}$	1	2	2
$\binom{1}{3}$	1	2	2
$\binom{2}{1}$	2	1	2
$\binom{2}{2}$	2	1	2
$\binom{2}{3}$	2	1	2
$\binom{3}{1}$	2	2	1
$\binom{3}{2}$	2	2	1
$\binom{3}{3}$	2	2	1

Table 4.2-2: *Number of times the ordered pairs of treatments appear in the sequences ending with t, for SBURMDs(3,6,9) with both $Z_1C_d^*$ and $Z_2C_d^*$ symmetric.*

If we consider the 72 symmetric SBURMDs(3,18,6) in Appendix L, there are 15 design which have $Z_2C_d^*$ symmetric. These are identified in Appendix L, where from Theorem 2.1-4, $\nu_1 = 2$ and $\nu_2 = 4$.

4.3 Comments on SBURMDs for t=4

From Section 2.2.4 Patterson (1973) gave eight non-isomorphic SBURMDs(4,16,8). These are four 'new' designs, with the other four being Quenouille's (1953) and Patterson's (1970) designs. Berenblut's (1964) construction of a SBURMD(4,16,8) is different to all of these eight designs, in that the sequences of treatments applied to the subjects are not the same, or the same under any permutation of the treatments, applied to the design. Hence there are nine SBURMDs(4,16,8) which have been constructed and these are presented in Tables 2.2-4 and 2.2-8.

If we were to consider construction of SBURMDs for t=4 in a similar manner to t=2 and 3, then there are $\frac{8!}{2!2!2!2!} = 2520$ sequences containing two 1's, two 2's, two 3's and two 4's. However these nine SBURMDs already constructed form a basis upon which to build larger SBURMDs for t=4 if required. Hence in the remainder of this chapter, only the properties of these nine SBURMDs will be considered for t=4.

4.3.1 Information Matrices

Table 4.3-1 contains the information matrices for direct treatment effects and residual treatment effects for any SBURMD(4,16s,8), s=1,2, with the additive linear model (1.3-1), calculated from Theorem 2.1.2.

t=4, n=16, p=8	t=4, n=32, p=8
$C_d = \begin{bmatrix} 24 & -8 & -8 & -8 \\ -8 & 24 & -8 & -8 \\ -8 & -8 & 24 & -8 \\ -8 & -8 & -8 & 24 \end{bmatrix}$	$C_d = \begin{bmatrix} 48 & -16 & -16 & -16 \\ -16 & 48 & -16 & -16 \\ -16 & -16 & 48 & -16 \\ -16 & -16 & -16 & 48 \end{bmatrix}$
$C_r = \begin{bmatrix} 20.625 & -6.875 & -6.875 & -6.875 \\ -6.875 & 20.625 & -6.875 & -6.875 \\ -6.875 & -6.875 & 20.625 & -6.875 \\ -6.875 & -6.875 & -6.875 & 20.625 \end{bmatrix}$	$C_r = \begin{bmatrix} 41.25 & -13.75 & -13.75 & -13.75 \\ -13.75 & 41.25 & -13.75 & -13.75 \\ -13.75 & -13.75 & 41.25 & -13.75 \\ -13.75 & -13.75 & -13.75 & 41.25 \end{bmatrix}$

Table 4.3-1: *Information matrices C_d and C_r for SBURMDs(4,16s,8), s=1,2.*

If a non-additive model is considered then the nine designs discussed for t=4 all have $Z_1C_d^*$ and $Z_2C_d^*$ symmetric. Hence, all of the designs previously constructed for t=4 have the residual treatment effects orthogonal to the direct treatment effects and the interaction of the direct and residual treatment effects.

4.3.2 Factorial Treatment Structure with SBURMDs

Instead of considering a single treatment classification for t=4, a 2 x 2 factorial structure could be considered. For example, instead of having four levels of one factor (t=1,2,3,4), two levels (say *1* and *2*) of two different factors (say *A* and *B*) could be considered. The non-additive linear model (1.3-1) would now have a 2 x 2 factorial structure in place of the direct treatment effects and the residual treatment effects. There would be a term for the main effect of *A* and of *B*, and a term for the interaction of *A* and *B*, in both the direct and residual treatment effects.

Applying a 2 x 2 factorial structure to SBURMDS(4,16,8) results in RMDs that retain the orthogonality between the direct and residual type treatment effects. Table 4.3-2 is an example of this using design d_1 from Table 2.2-8. If we consider the *A* factor combination only in this example, the number of times A_1 appears as one of the treatment combinations followed by a period where A_1 is also applied is 28. Similarly, if we considered the ordered pairs (A_1,A_2), (A_2,A_1), (A_2,A_2), the number of times that each of these exists is also 28. If we consider the *B* factor combinations only, then the number of times that the ordered pairs (B_1,B_1), (B_1,B_2), (B_2,B_1), (B_2,B_2) follow one and other is also 28. If both factors *A* and *B* are considered, the number of times the ordered pairs (A_1B_1,A_1B_1), (A_1B_1,A_1B_2), (A_1B_1,A_2B_1), (A_1B_1,A_2B_2), (A_1B_2,A_1B_1), ..., (A_1B_2,A_2B_2), ..., ..., (A_2B_2,A_1B_1) , ..., (A_2B_2,A_2B_2) follow one another is 7.

That is, each treatment combination follows each other treatment combination (including itself) the same number of times, for each of the two main effects and the interaction. Hence, the properties of orthogonality pertaining to the SBURMDs also apply when a factorial treatment structure is used. In such cases where a factorial structure has been applied to a SBURMD(t,n,p), we will denote this design as a SBURMD(t_1 x t_2, n,p), as all properties of the SBURMDs still remain.

Period	Subject 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
1	A_1B_1	A_1B_1	A_1B_2	A_1B_2	A_2B_1	A_2B_1	A_2B_2	A_2B_2	A_1B_1	A_2B_1	A_1B_1	A_2B_2	A_1B_2	A_2B_2	A_2B_1	A_1B_2
2	A_1B_1	A_1B_2	A_1B_2	A_2B_1	A_2B_1	A_2B_2	A_2B_2	A_1B_1	A_2B_1	A_1B_1	A_2B_2	A_1B_2	A_2B_2	A_2B_1	A_1B_2	A_1B_1
3	A_1B_2	A_1B_2	A_2B_1	A_2B_1	A_2B_2	A_2B_2	A_1B_1	A_1B_1	A_1B_1	A_2B_2	A_1B_2	A_2B_2	A_2B_1	A_1B_2	A_1B_1	A_2B_1
4	A_1B_2	A_2B_1	A_2B_1	A_2B_2	A_2B_2	A_1B_1	A_1B_1	A_1B_2	A_2B_2	A_1B_2	A_2B_2	A_2B_1	A_1B_2	A_1B_1	A_2B_1	A_1B_1
5	A_2B_1	A_2B_1	A_2B_2	A_2B_2	A_1B_1	A_1B_1	A_1B_2	A_1B_2	A_1B_2	A_2B_2	A_2B_1	A_1B_2	A_1B_1	A_2B_1	A_1B_1	A_2B_2
6	A_2B_1	A_2B_2	A_2B_2	A_1B_1	A_1B_1	A_1B_2	A_1B_2	A_2B_1	A_2B_2	A_2B_1	A_1B_2	A_1B_1	A_2B_1	A_1B_1	A_2B_2	A_1B_2
7	A_2B_2	A_2B_2	A_1B_1	A_1B_1	A_1B_2	A_1B_2	A_2B_1	A_2B_1	A_2B_1	A_1B_2	A_1B_1	A_2B_1	A_1B_1	A_2B_2	A_1B_2	A_2B_2
8	A_2B_2	A_1B_1	A_1B_1	A_1B_2	A_1B_2	A_2B_1	A_2B_1	A_2B_2	A_1B_2	A_1B_1	A_2B_1	A_1B_1	A_2B_2	A_1B_2	A_2B_2	A_2B_1

Table 4.3-2: *A SBURMD(2x2,16,8).*

Fletcher and John (1985) considered the construction of RMDs with factorial structures. The merits of orthogonality in RMDs were discussed in relation to confounding between parameters. The desirability of orthogonality of direct treatment effects to both subject and period effects was also discussed along with the desirability of orthogonality between direct and residual treatment effects. Fletcher and John also pointed out that RMDs based upon SBURMDs with a factorial structure applied are often too large for practical use. However, for an optimal 2 x 2 factorial structure, 16 subjects and 8 periods are required, which might be manageable, depending on what 'subjects' and 'periods' are.

Fletcher and John (1985), then considered 'smaller' RMDs that could take a factorial treatment structure. The construction of these designs is discussed in great detail and followed up by Fletcher (1987), Lewis, Fletcher and Matthews (1988), and Fletcher, Lewis and Matthews (1990). However, as these designs do not consider the notion of strongly balanced RMDs and orthogonality between direct and residual treatment effects, the constructions are not given here. These design are discussed further in Section 5.2.3.

Chapter 5 Conclusions

The SBURMDs constructed in Chapters 3 and 4 can now be used as 'building blocks' to construct larger SBURMDs for a given number of treatments, and will still have orthogonality. These larger SBURMDs are discussed in Section 5.1. However, it is not always true that sufficient resources are available to use SBURMDs. Problems include the lack of subjects in a clinical trial and the number of periods for which an experiment can be run. Other smaller, optimal RMDs exist for the estimation of direct, and of residual, treatment effects. These are based on SBURMDs, and BURMDs with extra periods added, and are discussed in Section 5.2. We also discuss alternative RMDs in which either direct or residual treatment effects are considered to be more important. Finally a summary of factorial treatment structures is presented. We conclude with analyses of the RMD of the Thornton *et al.*, (1987) example discussed in Section 1.1, as an indication of the application of the issues raised in this thesis.

5.1 Vertical and Horizontal Pasting of SBURMDs

The 'smallest' SBURMDs of Chapters 3 and 4 for a given number of treatments can be used as 'building blocks' to construct larger SBURMDs. For example see Section 2.3.2, and Theorem 3.3-1, relating to t=2. The vertical and horizontal pasting discussed in Theorem 3.3-1 can also be extended to any SBURMDs for any number of treatments.

Hence, for t=2, SBURMDs(2,4s,p), p=4,6,8,10,..., s=1,2,3,..., can be constructed by considering the SBURMDs(2,4s,4) in Table 3.1-3 and the SBURMDs(2,4s,6) in Table 3.2-3, with the appropriate horizontal or vertical pasting. For t=3, the SBURMDs(3,9,6) in Appendix K, the SBURMD(3,9,9) design produced by Sen and Mukerjee's (1987) construction given in Section 2.2.3, and Quenouille's (1953) SBURMDs(3,18,9) in Table 2.2-2, can be used appropriately to produce SBURMDs(3,9s,p), p=6,9,12,15,..., s=1,2,3,... .

If the non-additive linear model is considered in connection with the vertical pasting of two SBURMDs which have direct, residual and interaction terms orthogonal, then the resulting SBURMD may also have these orthogonality properties, if Theorem 2.1-4 is considered. For example, consider the following, where two SBURMDs(3,9,6) with $Z_1C_d^*$ and $Z_2C_d^*$ symmetric, are vertically pasted to produce a SBURMD(3,9,12) with $Z_1C_d^*$ and $Z_2C_d^*$ symmetric.

Example 5.1-1

Consider d_3 and d_4 from Appendix K

d_3
1 2 3 1 2 3 1 2 3
1 2 3 1 2 3 3 1 2
2 3 1 3 1 2 2 3 1
2 3 1 2 3 1 2 3 1
3 1 2 3 1 2 3 1 2
3 1 2 2 3 1 1 2 3

d_4
1 2 3 1 2 3 1 2 3
1 2 3 1 2 3 3 1 2
2 3 1 2 3 1 2 3 1
2 3 1 3 1 2 3 1 2
3 1 2 3 1 2 2 3 1
3 1 2 2 3 1 1 2 3

Both of these SBURMDs(3,9,6) have the number of ordered pairs for each sequence ending with 1, 2 and 3 as in Table 4.2-2, that is the orthogonality property holds. When these two designs are vertically pasted to produce a SBURMD(3,9,12), it can be done in such a manner that Theorem 2.1-4 still holds. That is the number of times that the ordered pairs appear are as given below.

Sequences ending in	Ordered Pairs $\binom{1}{1}$	$\binom{1}{2}$	$\binom{1}{3}$	$\binom{2}{1}$	$\binom{2}{2}$	$\binom{2}{3}$	$\binom{3}{1}$	$\binom{3}{2}$	$\binom{3}{3}$
1	3	3	3	4	4	4	4	4	4
2	4	4	4	3	3	3	4	4	4
3	4	4	4	4	4	4	3	3	3

#

5.2 Other RMDs

5.2.1 Optimal Designs in the Estimation of Direct and Residual Effects

This thesis has been concerned with the construction of RMDs which are universally optimal in the estimation of direct and residual treatment effects. Cheng and Wu (1980, Theorem 3.1) proved that SBURMDs are universally optimal in the estimation of direct and residual treatment effects. They also showed that SBURMDs(t,n,p) exists for $t|p$, $t|n$, $t^2|(p-1)n$ and pt^{-1} an even integer (Theorem 3.2). Sen and Mukerjee (1987) showed that SBURMDs(t,n,p) exist as above with pt^{-1} an odd integer.

SBURMDs also have the properties of orthogonality as discussed in Section 2.1.2. However, SBURMDs often have the drawback of requiring too many experimental units. Lucas (1957) first introduced the idea of repeating the observations in the last period. Cheng and Wu (1980, Theorem 3.3 and Corollary 3.3.1) use this idea to prove that there are other RMDs which have the property of universal optimality in the estimation of both direct and residual

treatment effects. Some of these designs are based on SBURMDs, whilst others are based upon BURMDs with extra periods added.

Theorem 5.2-1 (From Cheng and Wu (1980, Theorem 3.3))

Let $n=\lambda_1 t$, $p=\lambda_2 t + 1$, $\lambda_1,\lambda_2 \geq 1$, and d^* be a strongly balanced RMD(t,n,p) which is uniform on the periods and is uniform on the units in the first p-1 ($=\lambda_1 t$) periods. Then d^* is universally optimal in the estimation of direct as well as residual effects over $\Omega_{t,n,p}$. #

Corollary 5.2-1 (From Cheng and Wu (1980, Corollary 3.3.1))

Let d^* be obtained by repeating the observations in the last period of a balanced uniform RMD(t,λ_1,t). Then d^* is universally optimal for the estimation of direct as well as residual effects over $\Omega_{t,n,p}$. #

Hence, using BURMDs, we can construct repeated measures designs which are universally optimal in the estimation of direct and residual treatment effects. Hedayat and Afsarinejad (1975, 1978) reported that BURMDs(t,t,t) exist for all even t; for odd t they do not exist for t=3,5,7, however, they exist for t=9,15,21,27,39,55,57. Williams (1949) and Sheehe and Bross (1961) proved that BURMDs(t,2t,t) always exist for t odd. The construction of these RMDs are given in Hedayat and Afsarinejad (1975, 1978).

Cheng and Wu (1980) also point out that designs satisfying the above Theorem can be constructed from SBURMDs. As $t^2|n$ an extra period can be added to the designs such that the resulting design is still strongly balanced, and satisfies the conditions for the Theorem.

Example 5.2-1

Consider the SBURMD(2,4,6) d_1 in Table 3.2-3, where the last period of the design is given by the treatments 2121. By Definition 1.2-2, the number of times that each treatment j follows each treatment i (i,j=1,2) in this design is 5 ($=m_{ij}$). By adding either 1122, 2211, 1221, 2112 as the treatments applied in the seventh period, then $m_{ij}=6$ (i,j=1,2), and the resulting design is strongly balanced, uniform on periods, and uniform in the first 6 (=p–1) periods on units. #

Hence using either SBURMDs; SBURMDs with an extra period; or BURMDs repeating the last period; it is possible to construct a large number of RMDs which are optimal in the estimation of direct and residual treatment effects. However, one thing to consider when using extra period designs is the fact that uniformity on units no longer exists and hence the direct treatment effects are no longer orthogonal to the subject effects. Table 5.2-1 gives the values of n and p for all RMDs that can be constructed with optimality for direct and residual treatment effects when t=2 and t=3.

Types of Optimal Designs		Using vertical and horizontal pasting and types of designs A,B and C, the dimensions of n and p for a given t for which optimal designs can be constructed.
t=2	A: SBURMD(t,t^2s,p) B: SBRMD($t,ts,t+1$) C : SBRMD($t,t^2s,p+1$) $s=1,2,3,...$, $p=4,6,8,10,...$	$n=4s$, $p=4,5,6,7,8,...$, $n=2s$, $p=3$ $s=1,2,3,...$.
t=3	A: SBURMD(t,t^2s,p) B: SBRMD($t,2ts,t+1$) C: SBRMD($t,t^2s,p+1$) $s=1,2,3,...$, $p=6,9,12,15,...$	$n=9s$, $p=6,7,9,10,12,13,...$, $n=6s$, $p=4$ $s=1,2,3,...$.
A: SBURMDs(t,n,p)		(pt^{-1} even or odd, $t\|p$, $t\|n$, $t^2\|(p-1)n$)
B: BURMD(t,λ_1,t) + last period repeated		-> SBRMD($t,\lambda_1,t+1$) $\lambda_1 \geq 1$ (uniform on periods and on units in 1st p-1 periods)
C: SBURMD(t,n,p) + extra period such that design is still strongly balanced		-> SBRMD($t,n,p+1$) (uniform on periods and on units in 1st p-1 periods)

Table 5.2-1: *RMDs universally optimal in the estimation of direct and residual treatment effects.*

Sen and Mukerjee (1987) claim that if we consider these optimal extra period designs and the non-additive model (1.3-2), then the residual effects are orthogonal to the direct effects and interaction, but that the direct effects are not necessarily orthogonal to the residual effects and direct by residual interaction, (i.e., the results for orthogonality of residual effects are robust, however results for the orthogonality of the direct treatment effects are non-robust). If we consider Example 5.2-1 with a non-additive linear model and Theorem 1.5-1, then we find that $Z_1C_d^*$ and $Z_2C_d^*$ are both symmetric when treatments 1122 are applied in period 7 to units 1,2,3,4 respectively. When treatments 2211 or 1221 are applied then $Z_1C_d^*$ and $Z_2C_d^*$ are not

symmetric. When treatments 2112 are applied $Z_1C_d^*$ is not symmetric and $Z_2C_d^*$ is symmetric. The matrices are given in Table 5.2-2, calculated using the Matlab program in Appendix B. Hence $Z_2C_d^*$ is not always symmetric, which is not what Sen and Mukerjee (1987) suggest.

	$Z_1C_d^*$	$Z_2C_d^*$
adding 1122	$3.4286\begin{bmatrix} 1 & 1 & -1 & -1 \\ 1 & 1 & -1 & -1 \\ -1 & -1 & 1 & 1 \\ -1 & -1 & 1 & 1 \end{bmatrix}$	$3\begin{bmatrix} 1 & -1 & 1 & -1 \\ -1 & 1 & -1 & 1 \\ 1 & -1 & 1 & -1 \\ -1 & 1 & -1 & 1 \end{bmatrix}$
2211	$\begin{bmatrix} 3.0714 & 3.5714 & -3.5714 & -3.0714 \\ 3.0714 & 3.5714 & -3.5714 & -3.0714 \\ -3.0714 & -3.5714 & 3.5714 & 3.0714 \\ -3.0714 & -3.5714 & 3.5714 & 3.0714 \end{bmatrix}$	$\begin{bmatrix} 2.5 & -3.0 & 3.5 & -3.0 \\ -2.5 & 3.0 & -3.5 & 3.0 \\ 2.5 & -3.0 & 3.5 & -3.0 \\ -2.5 & 3.0 & -3.5 & 3.0 \end{bmatrix}$
1221	$\begin{bmatrix} 2.8571 & 3.7857 & -3.3571 & -3.2857 \\ 2.8571 & 3.7857 & -3.3571 & -3.2857 \\ -2.8571 & -3.7857 & 3.3571 & 3.2857 \\ -2.8571 & -3.7857 & 3.3571 & 3.2857 \end{bmatrix}$	$\begin{bmatrix} 2.5 & -3.0 & 3.5 & -3.0 \\ -2.5 & 3.0 & -3.5 & 3.0 \\ 2.5 & -3.0 & 3.5 & -3.0 \\ -2.5 & 3.0 & -3.5 & 3.0 \end{bmatrix}$
2112	$\begin{bmatrix} 3.6429 & 3.2143 & -3.6429 & -3.2143 \\ 3.6429 & 3.2143 & -3.6429 & -3.2143 \\ -3.6429 & -3.2143 & 3.6429 & 3.2143 \\ -3.6429 & -3.2143 & 3.6429 & 3.2143 \end{bmatrix}$	$3\begin{bmatrix} 1 & -1 & 1 & -1 \\ -1 & 1 & -1 & 1 \\ 1 & -1 & 1 & -1 \\ -1 & 1 & -1 & 1 \end{bmatrix}$

Table 5.2-2: *$Z_1C_d^*$ and $Z_2C_d^*$ for extra-period designs based on a SBURMD(2,4,6).*

Kok and Patterson (1976) suggested ways of finding or checking extra period design which were R-orthogonal (discussed in Section 2.1.2.b and Appendix D). This method is in fact the same as suggest by Sen and Mukerjee (1987) in Theorem 2.1-4, except that the number of times each treatment combination appears in each of the sequences ending in i (i=1,2,...,t) are now the same. This is demonstrated as follows.

Example 5.2-2

Design d_1 from Table 3.2-3:

1 1 2 2
1 2 1 2
1 1 2 2
2 2 1 1
2 2 1 1
2 1 2 1

By adding an extra period of (a) 1 1 2 2, (b) 2 2 1 1, (c) 1 2 2 1, (d) 2 1 1 2, a SBRMD(2,4,7) is obtained which satisfies Theorem 5.5-1

If the non-additive linear model 1.3-2 is considered then only the design obtained by pasting (a) has both $Z_1C_d^*$ and $Z_2C_d^*$ symmetric. This can be seen by counting the

number of times the ordered pairs (1,1), (1,2), (2,1) and (2,2) appear in each of the new designs in the sequences ending with 1 and the sequences ending in 2.

		Adding to make period 7								
		a)		b)		c)		d)		
ordered pairs	Sequences ending with t=	1	2	1	2	1	2	1	2	
$\binom{1}{1}$		3	3	2	4	2	4	2	4	
$\binom{1}{2}$		3	3	2	4	2	4	4	2	
$\binom{2}{1}$		3	3	4	2	4	2	5	1	
$\binom{2}{2}$		3	3	4	2	4	2	1	5	#

If we consider all other SBURMDs(2,4,6) in Table 3.2-3, and add all possible extra periods such that Theorem 5.1-1 holds, we find that the only way to construct these designs such that there is orthogonality between the direct treatment effects, the residual treatment effects and the interaction is to add the extra period as follows. For designs $d_1,d_2,d_3,...,d_8,d_{12},d_{15}$ add 1122 as the treatments applied in period 7 to units 1,2,3,4. For designs d_9,d_{10} add 2211 as the treatments in period 7. It should however be noted that designs d_{11}, d_{13} and d_{14} cannot have an extra period added such that $Z_1C_d^*$ and $Z_2C_d^*$ are symmetric.

5.2.2 Optimal Designs in the Estimation of Either Direct Or Residual Treatment Effects

Street, Eccleston and Wilson (1990) tabulate optimal repeated measures designs for the estimation of direct, and of residual, effects for the linear model 1.3-1. For t=2, n=4,5,...,10, and p=2,3,4, and for t=3, n=5,6,...,10, and p=2,3, they have tabulated about 5 designs for each set of values which are optimal for direct (residual) treatment effects whilst remaining 'reasonable' for the residual (direct) effects.

For t=2, their definition of reasonable involves selecting lower bounds on the traces of the information matrices C_d and C_r, defined in Section 1.4. Here the 'best' designs in both categories for t=2,n=4,8, and p=4 are the SBURMDs given in Table 3.1-3, as they are universally optimal in the estimation of both the direct and residual treatment effects. From Street *et al* ., (1990), for t=2, n=4, and p=3, one design is 'best' for both the direct treatment effects and residual treatment effects. This design is given here in Table 5.2-3. In fact this design is strongly balanced and uniform in the first 2 (= p–1) periods and hence, is universally

optimal in the estimation of the direct and residual treatment effects, by Theorem 5.2-1. This design can be constructed by considering the BURMD(2,2,2) and repeating the last period and horizontally pasting this design twice.

1	2	1	2
2	1	2	1
2	1	2	1

Table 5.2-3: *Optimal RMD(2,4,3) for both direct and residual treatment effects.*

For t=3, their definition of reasonable consists of calculating the A-optimal values associated with each design for direct and residual treatment effects. (A-optimality is used here instead of maximum trace of the information matrices, because, as Street *et al.*, (1990) point out, the information matrices C_d and C_r are not necessarily completely symmetric which may lead to design with maximum trace not being universally optimal.)

Hence, these tables can be used to obtain optimal RMDs(t,n,p), for small values of t,n, and p. This provides designs in such instances where the number of experimental units and number of periods are limited.

5.2.3 Factorial RMDs

As discussed in Section 4.3.2, a factorial treatment structure can be applied to SBURMDs. Fletcher and John (1985) discuss factorial treatment structures applied to RMDs with smaller 'dimensions'. The choice of designs in this case depend on whether the interaction is likely to be important.

Fletcher (1987) gives a means of calculating the cannonical efficiency factors for treatment, direct and residual effects, and applies this to give RMDs with high efficiency values for generalized cyclic change-over designs for two factor and three factor experiments. The designs tabled are for a 2 x 2 factorial treatment structure with p=3,4, and n=4,8; 2 x 3 with p=4,5,6 and n=6,12; 2 x 4 with p=4,5,6 and n=8,16; 3 x 3 with p=4,5,6 and n=9,18,27; and 4 x 4 with p=5,6 and n=16,32,48. Each cannonical efficiency factor provides a measure of the variance with which the corresponding basic contrast is estimated. However, while these designs may have good efficiency for estimating main effects, they may not be adequate for an interaction term.

Lewis *et al.*, (1988) extended this idea to produce RMDs which can be used as 'bricks' to build up efficient designs. Again the cannonical efficiency factors are given for RMDs but the number of designs in each class has been extended. They also introduce the idea of the 'bonus' efficiency factor which indicates the gain in efficiency by using more than one design from a class to build up a larger design. They point out that it is better to combine different 'bricks' rather than repeat a single one, and that in practice the bonus may be small but it is not always the case. In Lewis *et al.*, (1987) and Fletcher *et al.*, (1990) the following designs were tabled, 2 x 2 with p=3,4; 2 x 3 with p=3,4; 2 x 4 with p=3,4; and 3 x 3 with p=3,4. These can then be used to produce designs for different numbers of subjects by horizontal pasting.

Lewis *et al.*, (1987) also point out that under certain experiments, one level of a factor could represent the absence of treatment . Under some circumstances, such as clinical drug trials on sick patients, this might be unethical and these designs are then no longer suitable.

5.3 Example of Analyses

If we again consider the Synthetic Octapeptide experiment of Thornton *et al.*, (1987), described in Section 1.1, then the data can be used as an example for analyses of RMDs. The data are given in Table 5.3-1, where treatment 1 represents the CCK-8 and 2 the Placebo.

Seq.	Subject																
S_1	10	8	S_2	1	2	S_3	12	3	S_4	4	6	S_5	5	9	S_6	11	7
1	360	263	1	715	887	1	558	531	2	521	610	2	659	517	2	378	538
1	416	139	2	1130	882	2	1427	525	1	466	471	1	664	444	2	449	449
2	519	401	2	1319	954	1	536	472	2	417	589	1	663	362	1	474	397
2	584	431	1	1483	582	2	1009	289	1	255	690	2	491	362	1	500	192

Table 5.3-1: *Food Intakes for the Synthetic Octapeptide Experiment - RMD(2,12,4).*

Using all 12 subjects, then the analysis of variance I in Table 5.3-2 can be obtained, where the Matlab program which appears in Appendix M was used to obtain the appropriate sums of squares. If the linear model 1.3-1 is considered then subject effects are not orthogonal to residual effects, direct effects are not orthogonal to residual effects and residual effects are not orthogonal to direct effects and subject effects. In addition, as there are two subjects per

sequence the subject effect can be partitioned up into a sequence effect and a subject within sequence effect. The linear model is then of the form

$$Y_{ij} = \mu + \alpha_i + \beta_j + \tau_{d(i,j)} + \rho_{d(i-1,j)} + E_{ij}, \qquad (5.3\text{-}1)$$

$$= \mu + \alpha_i + \psi_r + \eta_{r(s)} + \tau_{d(i,j)} + \rho_{d(i-1,j)} + E_{ij}$$

$$i = 1,2,...,4\ , \quad j = 1,2,...,12, \quad r=1,2,...,6, \quad s=1,2, \quad \mathrm{Var}\,(E_{ij}) = \sigma^2, \quad \rho_{d(0,jk)} = 0,$$

where α,β,τ and ρ are the period, subject, direct treatment, and residual treatment effects respectively (as before) with ψ the r^{th} sequence effect and η the effect of the s^{th} subject within the r^{th} sequence.

I - AOV for ln(food intake) - RMD(2,12,4)				
source	df	SS	MS	F
period	3	0.0860	0.0287	0.35
subject (adjusted for residual effect)	11	6.6090	0.6008	7.29
sequence (adj for res effect)	5	4.5149	0.9030	2.59
subject within sequence	6	2.0941	0.3490	4.26
direct (adjusted for residual effect)	1	0.8288	0.8288	10.06
residual (adjusted for residual and subject effects)	1	0.2477	0.2477	3.01
error	31	2.5541	0.0824	
total	47	10.3246		

II - AOV for ln(food intake) - SBURMD(2,8,4)				
source	df	SS	MS	F
period	3	0.1260	0.0420	0.59
subject (adjusted for residual effect)	7	5.1839	0.7406	10.46
sequence	3	4.1107	1.3702	5.11
subject within sequence	4	1.0732	0.2683	3.79
direct	1	0.4398	0.4398	6.21
residual (adjusted for subject effect)	1	0.3132	0.3132	4.42
error	19	1.3447	0.0708	
total	31	7.8053		

Table 5.3-2: *Analyses of Variance for Synthetic Octapeptide Experiment.*

As Thornton *et al.*, (1987) also point out, instead of using all 6 sequences it would have been better to use the SBUMD(2,4,4) of Table 2.2-1, and have 3 subjects on each of these four sequences, as briefly discussed in Section 2.3. As an indication only, the data from sequences S_1, S_2, S_5 and S_6 which make up the SBURMD are also analysed and appear as analysis of variance II in Table 5.3-2. For a full summary and discussion of the analyses and the conclusions see Thornton *et al.*, (1987).

5.4 Summary

From Theorem 1.3-1, we have seen that if we consider the additive linear model 1.3-1 that SBURMDs are universally optimal in the estimation of the direct and residual treatment effects. If the non-additive linear model 1.3-2 is considered, from Theorem 2.1-3, a SBURMD is universally optimal for the estimation of direct effects; however, by Theorem 2.1-4, the SBURMD does not necessarily have universal optimality in the estimation of the residual treatment effects.

Sen and Mukerjee (1987) discussed examples where SBURMDs with the non-additive linear model are universally optimal in the estimation of both direct and residual treatment effects. That is, where there is orthogonality between the direct treatment effects, the residual treatment effects, and the direct by residual treatment interaction. Theorem 2.1-4 gives a means of identifying those SBURMDs with residual treatment effects orthogonal to both the direct treatment effects and the interaction, which is equivalent to $Z_1C_d^*$ and $Z_2C_d^*$ of Section 1.5 both being symmetric.

As discussed in Chapter 2, there are a limited number of SBURMDs that can be constructed by the methods given in the literature for small numbers of treatments. In Chapters 3 and 4 we have discussed ways of constructing SBURMDs for t=2 and 3, with the minimum requirements which satisfy the conditions for strong balance and uniformity. The SBURMDs in Chapters 3 and 4 can then be used as 'building blocks' to produce larger SBURMDs for the given number of treatments.

However, because of the nature of some experimental units or the limitations under which an experiment is to be conducted, it is not always possible to use SBURMDs. Other

optimal RMDs for the estimation of direct and residual treatment effects exist using SBURMDs and BURMDs with extra periods added.

This thesis provides a basis from which to select or construct RMDs to provide the most information about the treatments under study. This includes the estimation of the direct and residual treatment effects, with, and without, subject number and time constraints, in the presence and absence of a non-additive term in the linear model. However, one should note that although some SBURMDs have both direct and residual effects orthogonal to the interaction term they only have universal optimality in the estimation of the direct and residual treatment effects. As Sen and Mukerjee (1987) remark, if optimal estimation of the interaction term is of interest, then further designs need to be investigated.

Appendix A: Calculating C_d and C_r using MATLAB

The following is a Matlab program to calculate C_d and C_r, where the notation `Dt` represents $\tilde{D}$, `Nut` represents $\tilde{N}_u$, and `Npt` represents $\tilde{N}_p$ from Section 1.5.

```
//    Matlab program calculating the information matrix for direct
//    treatment effects (Cd) and the information matrix for the residual
//    treatment effects (Cr) as in Section 1.4, for any RMD given as a
//    p x n array, with elements 1...t used to represent the elements in d.
//    Written by S.J. Pattison Aug 1990.

<p,n> = size(d)
t = max(d)

dd =  0*J(t,1);
ddt = 0*J(t,1);
M = 0*J(t,t);
Np = 0*J(t,p);
Nu = 0*J(t,n);
Nut = 0*J(t,n);

for i = 1:p, for j = 1:n,..
   row = d(i,j);..
   dd(row,1) = dd(row,1) + 1;..
   Np(row,i) = Np(row,i) + 1;..
   Nu(row,j) = Nu(row,j) + 1;..
end;
D = diag(dd);

for i = 1:p-1, for j = 1:n,..
   row = d(i,j);..
     ddt(row,1) = ddt(row,1) + 1;..
     Nut(row,j) = Nut(row,j) + 1;..
   row = d(i+1,j); col = d(i,j);..
     M(row,col) = M(row,col) + 1;..
end;
Dt = diag(ddt);

Npt = [ 0*J(t,1) Np(:,1:p-1) ];

C11 = D - 1/n*Np*Np'   - 1/p*Nu*Nu'   + 1/(n*p)*Nu*J(n,n)*Nu'   ;
C12 = M - 1/n*Np*Npt'  - 1/p*Nu*Nut'  + 1/(n*p)*Nu*J(n,n)*Nut'  ;
C22 = Dt - 1/n*Npt*Npt' - 1/p*Nut*Nut' + 1/(n*p)*Nut*J(n,n)*Nut';
C21 = C12';

Cd = C11- C12*(pinv(C22))*C21
Cr = C22- C21*(pinv(C11))*C12
```

Appendix B: Calculating $Z_1C_d^*$ and $Z_2C_d^*$ using MATLAB

```
//    General Matlab program to calculate Z1Cd* and Z2Cd* from Section 1.5,
//   for a given design d, with known t, n and p, as in Sen and Mukerjee
//    (1987), to see if residual treatment effects are orthogonal to direct
//    by residual treatment interaction.
//    For SBURMDs the direct treatment effects are orthogonal to direct by
//    residual treatment interaction (Z1Cd* is symmetric) but residual
//    treatment effects are not necessarily orthogonal to the interaction.
//    Written by S.J. Pattison Aug, 1990.

<p,n> = size(d);
t = max(d);
t2 = t*t;

//      Column i of e is ei ( a tx1 vector with 1 in the ith position and
//      zeros elsewhere).
e = I(t);

//      Calculating lambda ij
for j = 1:n,..
     L(1:t2,j) = (e(:,d(1,j)).*.J(t,1))/t;, end
for i = 2:p, for j = 1:n,..
     L((i-1)*t2+1:i*t2,j) = (e(:,d(i,j)).*.e(:,d(i-1,j)));, end


//      Calculating Md
for j = 1:n, Md(1:t2,j) = 0*J(t2,1);, for i = 1:p,..
     Md(1:t2,j) = Md(1:t2,j)+L((i-1)*t2+1:i*t2,j);,end;

//      Calculating Nd
for i = 1:p, Nd(1:t2,i) = 0*J(t2,1);, for j = 1:n,..
     Nd(1:t2,i) = Nd(1:t2,i)+L((i-1)*t2+1:i*t2,j);,end;

//      Calculating Vd
Vd = 0*J(t2,t2);
for i = 1:p, for j= 1:n,..
    Vd = Vd + (L((i-1)*t2+1:i*t2,j)*L((i-1)*t2+1:i*t2,j)');,end;


Cd = Vd - 1/n*(Nd*Nd') - 1/p*(Md*Md') + 1/(n*p)*((Nd*J(p,1))*(Nd*J(p,1))');
Z1 = I(t).*.(J(t,1)*J(t,1)') ;
Z2 = (J(t,1)*J(t,1)').*.I(t) ;

A=Z1*Cd;  AA=(Z1*Cd)';  symA = A-AA;
B=Z2*Cd;  BB=(Z2*Cd)';  symB = B-BB;
d,Cd,A,B
```

Appendix C: Proof of Theorem 2.1-2

Let I_p be the identity matrix of size p and $J_{p,n}$ a p x n matrix of ones, then for any SBURMD(t,n,p) the matrices in Section 1.4 generalise to the following.

$$D = \frac{np}{t} I_t, \qquad \tilde{D} = \frac{n(p-1)}{t} I_t, \qquad M = \frac{n(p-1)}{t^2} J_{t,t}, \qquad N_p = \frac{n}{t} J_{t,p},$$

$$\tilde{N}_p = \frac{n}{t} [0.J_{t,1} \; J_{t,p-1}], \qquad N_u = \frac{p}{t} J_{t,n}, \text{ and } \qquad \tilde{N}_u = (\frac{p}{t} J_{t,t} - I_t) \otimes J_{1,n/t}.$$

Now from Section 1.4

$$C_{11} = D - n^{-1} N_p N_p^T - p^{-1} N_u N_u^T + (np)^{-1} N_u J_{n,n} N_u^T,$$

$$C_{12} = C_{21}^T = M - n^{-1} N_p \tilde{N}_p^T - p^{-1} N_u \tilde{N}_u^T + (np)^{-1} N_u J_{n,n} \tilde{N}_u^T,$$

and

$$C_{22} = \tilde{D} - n^{-1} \tilde{N}_p \tilde{N}_p^T - p^{-1} \tilde{N}_u \tilde{N}_u^T + (np)^{-1} \tilde{N}_u J_{n,n} \tilde{N}_u^T.$$

Using D, $\tilde{D}$, etc. from above they become the following.

$$\begin{aligned} C_{11} &= \frac{np}{t} I_t - \frac{np}{t^2} J_{t,t} - \frac{np}{t^2} J_{t,t} - \frac{np}{t^2} J_{t,t} \\ &= \frac{np}{t} \left(I_t - \frac{1}{t} J_{t,t} \right) = \frac{t-1}{t} \cdot \frac{np}{t} \left(\frac{t}{t-1} I_t - \frac{1}{t-1} J_{t,t} \right) \\ &= \frac{(t-1)np}{t^2} \left(I_t + \frac{1}{t-1} (I_t - J_{t,t}) \right) \end{aligned}$$

$$\begin{aligned} C_{12} &= C_{21}^T = \frac{n(p-1)}{t^2} J_{t,t} - \frac{n(p-1)}{t^2} J_{t,t} - \frac{n}{t^2} \left(\frac{2p}{t} - 1 \right) J_{t,t} + \frac{n}{t^2} \left(\frac{2p}{t} - 1 \right) J_{t,t} \\ &= (0) J_{t,t} \end{aligned}$$

$$\begin{aligned} C_{22} &= \frac{n(p-1)}{t} I_t - \frac{n(p-1)}{t^2} J_{t,t} - \frac{n}{pt} \left(\frac{p(p-2)}{t} J_{t,t} + I_t \right) + \frac{n(p-1)^2}{pt^2} J_{t,t} \\ &= \frac{n(p^2-p-1)}{pt} \left(I_t - \frac{1}{t} J_{t,t} \right) \\ &= \frac{n(t-1)(p^2-p-1)}{pt^2} \left(I_t + \frac{1}{t-1} (I_t - J_{t,t}) \right) \end{aligned}$$

Then from (1.4-1) and (1.4-2), $C_d = C_{11}$ and $C_r = C_{22}$, and hence the result follows.

Appendix D: R-Orthogonal Designs

The following are the matrices associated with R-orthogonal designs from Kok & Patterson (1976) for SBURMDs($t,t^2,2t$) when considering a non-additive model, as discussed in Section 2.1.1.b.

Let X_i be a n x t first order incidence matrix, where element (k,q) is one if subject k receives treatment q in period i and zeros elsewhere, $1 \le i \le 2t$, $1 \le k \le t^2$, $1 \le q \le t$,

and X_{ij} be a n x n second order incidence matrix, where element (k,qr) is one if subject k receives treatment q in period i and r in period j and zeros elsewhere, $1 \le k \le t^2$, $1 \le q,r \le t$, $1 \le i,j \le 2t$.

Then $X_{ij} = (X_i \otimes J_{1,t}).(J_{1,t} \otimes X_i)$,

$$X_{10} = \frac{1}{t}(X_1 \otimes J_{1,t})$$

and

$$N = \sum_{i=2}^{2t} X_{i,i-1}^T,$$ which determines the incidence pairs of treatments in consecutive periods.

Now let

$$L = \left(I_t \otimes \frac{J_{t,t}}{t}\right) + (2t-1)\, I_n - \frac{1}{2t}\left(N + X_{10}^T\right)\left(N^T + X_{10}\right),$$

$$T_0 = \frac{J_{t,t}}{t} \otimes \frac{J_{t,t}}{t},$$

$$T_1 = \left(I_t - \frac{J_{t,t}}{t}\right) \otimes \frac{J_{t,t}}{t},$$

$$T_2 = \frac{J_{t,t}}{t} \otimes \left(I_t - \frac{J_{t,t}}{t}\right),$$

and

$$T_{12} = \left(I_t - \frac{J_{t,t}}{t}\right) \otimes \left(I_t - \frac{J_{t,t}}{t}\right).$$

Then $T_1 L = 2tT_1$ in designs which have

i) every ordered pair of treatments given to exactly one subject in every two consecutive periods, and

ii) every subject receives each treatment twice in the course of 2t periods.

That is the columns of T_1 are eigenvectors of L. So $T_1LT_2 = 0$ and $T_1LT_{12} = 0$, implying that direct treatment effects are orthogonal to residual treatment effects and the direct by residual treatment interaction. However, residual treatment effects are orthogonal to the interaction if and only if $T_2LT_{12} = 0$. That is designs are only R-orthogonal if and only if the columns of T_2 are eigenvectors of L.

Example

Consider the RMD(2,4,4) d_2 in Table 1.2-1, which is neither uniform on rows nor columns but is strongly balance by Definition 1.2-2.

Then

$$X_1 = \begin{bmatrix} 1 & 1 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix}, \quad X_2 = \begin{bmatrix} 1 & 0 & 0 & 1 \\ 0 & 1 & 1 & 0 \end{bmatrix}, \quad X_3 = \begin{bmatrix} 0 & 0 & 0 & 1 \\ 1 & 1 & 1 & 0 \end{bmatrix}, \text{ and } X_4 = \begin{bmatrix} 0 & 1 & 1 & 1 \\ 1 & 0 & 0 & 0 \end{bmatrix}.$$

$$L = \begin{bmatrix} 1.8125 & -0.5625 & -0.8750 & -0.8750 \\ -0.5625 & 2.0625 & -1.0000 & -1.0000 \\ -0.8750 & -1.0000 & 2.6875 & -0.3125 \\ -0.8750 & -1.0000 & -0.3125 & 2.6875 \end{bmatrix}, \quad T_1LT_2 = 0.0313 \begin{bmatrix} -1 & 0 & -1 & 0 \\ -1 & 0 & -1 & 0 \\ 0 & -1 & 0 & -1 \\ 0 & -1 & 0 & -1 \end{bmatrix},$$

$$T_1LT_{12} = 0.0313 \begin{bmatrix} -1 & 0 & -1 & 0 \\ -1 & 0 & -1 & 0 \\ 0 & -1 & -1 & 0 \\ 0 & -1 & -1 & 0 \end{bmatrix}, \quad \text{and} \quad T_2LT_{12} = 0.0625 \begin{bmatrix} -1 & 0 & 0 & -1 \\ 0 & -1 & -1 & 0 \\ -1 & 0 & 0 & -1 \\ 0 & -1 & -1 & 0 \end{bmatrix}.$$

This indicates that the direct treatment effects are not orthogonal to the residual treatment effects and the interaction, and that the residual treatment effects are not orthogonal to the interaction term. This is comparable with calculating $Z_1C_d^*$ and $Z_2C_d^*$ (Sen and Mukerjee (1987)) from Section 1.5. These two matrices are not symmetric, and are given as follows.

$$Z_1C_d^* = \begin{bmatrix} 1.6250 & 1.8750 & -2.1250 & -1.3750 \\ 1.6250 & 1.8750 & -2.1250 & -1.3750 \\ -1.6250 & -1.8750 & 2.1250 & 1.3750 \\ -1.6250 & -1.8750 & 2.1250 & 1.3750 \end{bmatrix}, \quad Z_2C_d^* = \begin{bmatrix} 0.5625 & -1.0625 & 1.6875 & -1.1875 \\ -0.5625 & 1.0625 & -1.6875 & 1.1875 \\ 0.5625 & -1.0625 & 1.6875 & -1.1875 \\ -0.5625 & 1.0625 & -1.6875 & 1.1875 \end{bmatrix}$$

Appendix E: Linear Equations for SBURMDs(2,4s,6)

The following are the set of linear equations used to find SBURMDs(2,4s,6), as discussed in Section 3.2.

Using Table 3.2-1, and the fact that designs are uniform on periods, we get

$$x_1 + x_2 + x_3 + x_4 + x_5 + x_6 + x_7 + x_8 + x_9 + x_{10} = \frac{n}{t} = 2s,$$

$$x_1 + x_2 + x_3 + x_4 + x_{11} + x_{12} + x_{13} + x_{14} + x_{15} + x_{16} = 2s,$$

$$x_1 + x_5 + x_6 + x_8 + x_{11} + x_{12} + x_{14} + x_{17} + x_{18} + x_{19} = 2s,$$

$$x_2 + x_5 + x_7 + x_9 + x_{11} + x_{13} + x_{15} + x_{17} + x_{18} + x_{20} = 2s,$$

$$x_3 + x_6 + x_7 + x_{10} + x_{12} + x_{13} + x_{16} + x_{17} + x_{19} + x_{20} = 2s,$$

$$x_4 + x_8 + x_9 + x_{10} + x_{14} + x_{15} + x_{16} + x_{18} + x_{19} + x_{20} = 2s.$$

Using Table 3.2-2, and the fact that the designs are strongly balanced, we get

$$2x_1 + x_2 + x_3 + x_4 + x_5 + x_7 + x_{10} + 2x_{11} + x_{12} + x_{13} + x_{14} + x_{16} + 2x_{17} + x_{18} + x_{19} + 2x_{20} = 5s,$$

$$x_1 + 2x_2 + 2x_3 + x_4 + 2x_5 + 3x_6 + 2x_7 + 2x_8 + 2x_9 + x_{10} + x_{11} + 2x_{12} + 2x_{13} + x_{14} + 2x_{15} + x_{16} + x_{17} + x_{18} + x_{19} = 5s,$$

$$x_2 + x_3 + x_4 + x_5 + 2x_6 + x_7 + 2x_8 + 2x_9 + x_{10} + x_{11} + 2x_{12} + 2x_{13} + 2x_{14} + 3x_{15} + 2x_{16} + x_{17} + 2x_{18} + 2x_{19} + x_{20} = 5s,$$

$$2x_1 + x_2 + x_3 + 2x_4 + x_5 + x_7 + x_8 + x_9 + 2x_{10} + x_{11} + x_{14} + x_{16} + x_{17} + x_{18} + x_{19} + 2x_{20} = 5s.$$

Appendix F: Finding SBURMDs(2,4,6)

a) Input file **data1** representing the matrix A and vector **b** from the set of linear equations in Appendix E, for t=2, n=4 and p=6, where A is selected such that it is of full row rank (rank(A) = 7).

```
2 1 1 1 1 0 1 0 0 1 2 1 1 1 0 1 2 1 1 2
0 1 1 1 1 2 1 2 2 1 1 2 2 2 3 2 1 2 2 1
1 1 1 1 1 1 1 1 1 1 0 0 0 0 0 0 0 0 0 0
1 1 1 1 0 0 0 0 0 0 1 1 1 1 1 1 0 0 0 0
1 0 0 0 1 1 0 1 0 0 1 1 0 1 0 0 1 1 1 0
0 1 0 0 1 0 1 0 1 0 1 0 1 0 1 0 1 1 0 1
0 0 1 0 0 1 1 0 0 1 0 1 1 0 0 1 1 0 1 1
5 5 2 2 2 2 2
```

b) A Pascal program called **p6t2n4.p** to find all SBURMDs(2,4,6)

```
{Program to find all strongly balanced, uniform RMD for p=6,t=2,n=4}
{Written by Sandra Pattison 28/3/89}

program p6t2n4(input,output,data1,p6t2n4);

var     A:array[1..7,1..20] of integer;
        b:array[1..7]       of integer;
        x:array[1..20]      of integer;
        d:array[1..7]       of integer;
        i,j,m,n,s  :integer;
        data1,p6t2n4              :text;


procedure    Read_A;          {Reads in the matrix A from data1}
var     i,j   :integer;
        begin       {Read_A}
        for i:=1 to 7 do
           begin
              for j:= 1 to 20 do read(data1,A[i,j]);
              readln(data1);
           end;
        end;        {Read_A}


procedure    Read_b;          {Reads in the vector b from data1}
var     i     :integer;
        begin             {Read_b}
        for i:=1 to 7 do
           begin
              read(data1,b[i]);
              b[i]:=b[i]*s;
           end;
        end;        {Read_b}
```

```
procedure    Mult;              {calculates Ax=d}
var     i,j   :integer;
        begin       {Mult}
        for i:=1 to 7 do
           begin
              d[i]:=0;
              for j:=1 to 20 do d[i]:=d[i]+A[i,j]*x[j];
           end;
        end;        {Mult}


procedure    Soln_Check;        {Checks to see if x is a solution to
                                 Ax=b, and if it is it's written to
                                 p6t2n4.}
var     ss,q,r:integer;
        begin       {Soln_Check}
        Mult;
        ss:=0;
        for q:=1 to 7 do ss:=ss+(d[q]-b[q])*(d[q]-b[q]);
        if ss=0 then
           begin
              for r:=1 to 20 do write(p6t2n4,x[r]:3);
              writeln(p6t2n4);
           end;
        end;        {Soln_Check}



begin   {main program}
s:=1;
reset(data1);
rewrite(p6t2n4);
Read_A;
Read_b;
for i:=1 to 20 do x[i]:=0;
for i:=1 to 10 do
   for j:= i to 10 do
         begin
            x[i]:=x[i]+1; x[j]:=x[j]+1;
            for m:=11 to 20 do
               for n:=m to 20 do
                     begin
                        x[m]:=x[m]+1; x[n]:=x[n]+1;
                        Soln_Check;
                        x[m]:=x[m]-1; x[n]:=x[n]-1;
                     end;
            x[i]:=x[i]-1; x[j]:=x[j]-1;
         end;
end. {program}
```

c) The output from p6t2n4.p in terms of the x_i's, i=1,2,...,20. These represent the number of times that each of the sequences S_i from Table 3.2-1 appear in a SBURMD(2,4,6).

x_1	x_2	x_3	x_4	x_5	x_6	x_7	x_8	x_9	x_{10}	x_{11}	x_{12}	x_{13}	x_{14}	x_{15}	x_{16}	x_{17}	x_{18}	x_{19}	x_{20}	
1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1	0	1	0	0	d_{11}
1	0	0	0	0	0	0	1	0	0	0	0	1	0	0	0	0	0	0	1	d_1
1	0	0	0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0	1	d_2
1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	1	1	0	0	0	d_{12}
1	0	0	0	0	0	0	0	0	1	0	0	1	0	0	0	0	1	0	0	d_{13}
1	0	0	0	0	0	0	0	0	1	0	0	0	0	1	0	1	0	0	0	d_{14}
0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	0	d_3
0	1	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	1	0	d_4
0	1	0	0	0	0	0	0	0	1	0	0	0	1	0	0	1	0	0	0	d_{15}
0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	d_5
0	0	1	0	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	$d_{11'}$
0	0	1	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	1	$d_{13'}$
0	0	1	0	0	0	0	0	0	1	1	0	0	0	0	0	0	1	0	0	d_6
0	0	0	1	1	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1	$d_{12'}$
0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	d_7
0	0	0	1	0	1	0	0	0	0	1	0	0	0	0	0	0	0	0	1	$d_{14'}$
0	0	0	1	0	0	1	0	0	0	1	0	0	0	0	0	0	0	1	0	$d_{15'}$
0	0	0	1	0	0	1	0	0	0	0	0	0	1	0	0	1	0	0	0	d_8
0	0	0	0	1	0	0	0	0	1	1	0	0	0	0	1	0	0	0	0	d_9
0	0	0	0	0	0	1	0	0	1	1	0	0	1	0	0	0	0	0	0	d_{10}

Designs $d_1,d_2,...,d_{10}$ are Symmetric Design and designs $d_{11},d_{12},...,d_{15}$ are Non-Symmetric Designs from Definition 3.2-1.

Designs $d_{i'}$ represent designs d_i , i = 11,12,...,15, with treatments permuted using (12).

Appendix G: Pascal Program to find SBURMDs(2,12,6) that come from n=4, and 8 Designs

```
{  Written by D.J.Street, S.J.Pattison 1 June 1989.

   Pascal program to find the non-isomorphic SBURMDs(2,12,6) which come
   from using either three n=4 designs; or one n=4 design and one n=8
   design. This is to see how many of the n=12 solutions in Table 3.2-4
   come from combinations of the other designs.

   (That is using the x_i's for t=2,n=4, and p=6 that appear in Appendix F
     (10 sym + 5 nonsym and their compliment) which are in the file p6t2n4
   and 3360 solutions for t=2,n=8, and p=6
     (388 sym + 1636 nonsym and their compliment) in a file called p6t2n8.
   The results are then printed in the file p6t2n12test.}


program p6t2n12test(input,output,p6t2n4,p6t2n8,p6t2n12test);

type    design   = array [1..20]   of integer;
        aa4      = array [1..20]   of design;
        aa8      = array [1..344]  of design;
        aa12     = array [1..4000] of design;

var     a4       : aa4;
        a8       : aa8;
        a12      : aa12;
        d,try,difference           : design;
        i,j,i4,i8,i12,count12      : integer;
        p6t2n4,p6t2n8,p6t2n12test  : text;
        new,zero : boolean;

procedure     a4read;                    {reads in designs of p=6 t=2 n=4}
   var     i,j     :integer;

   begin
   reset(p6t2n4);
   for  i := 1 to 20 do
      begin
         for j := 1 to 20 do  read(p6t2n4,d[j]);
         a4[i] := d;
      end;
   end;


procedure     a8read;                    {reads in designs of p=6 t=2 n=8}
   var     i,j     :integer;

   begin
   reset(p6t2n8);
   for  i := 1 to 344 do
      begin
         for j := 1 to 20 do  read(p6t2n8,d[j]);
         a8[i] := d
      end;
   end;


begin                                     {main program}
rewrite(p6t2n12test);
a4read;
a8read;
```

```
for i := 1 to 20 do
   a12[1][i] := a4[1][i] + a8[1][i];
count12 := 1;
for i4 := 1 to 20 do
   for i8 := 1 to 344 do
      begin
        for i := 1 to 20 do
           try[i] := a4[i4][i] + a8[i8][i];
        new := true;
        i12 := 1;
        while new and (i12 <= count12) do
           begin
              for i := 1 to 20 do
              difference[i] := try[i] - a12[i12][i];
              zero := true;
              for j := 1 to 20 do
                 zero := zero and (difference[j] = 0);
              if (zero = true)
                then new := false
                else i12 := i12+1;
           end;
        if (i12 > count12) and new then
           begin
              count12 := count12 + 1;
              for i:= 1 to 20 do
              a12[count12][i] := try[i];
           end;
      end;

   for i12 := 1 to count12 do
      begin
        for j := 1 to 20 do write(p6t2n12test,a12[i12][j]:3);
        writeln(p6t2n12test);
      end;
end.                                          {main program}
```

Appendix H: C_d^*, $Z_1C_d^*$ and $Z_2C_d^*$ for all SBURMDs(2,4,6)

The matrices C_d^*, $Z_1C_d^*$ and $Z_2C_d^*$ from Section 1.5, appear here for the fifteen SBURMDs(2,4,6) from Table 3.2-3, calculated using the Matlab program from Appendix B, where $A = \begin{bmatrix} 1 & 1 & -1 & -1 \\ 1 & 1 & -1 & -1 \\ -1 & -1 & 1 & 1 \\ -1 & -1 & 1 & 1 \end{bmatrix}$ and $B = \begin{bmatrix} 1 & -1 & 1 & -1 \\ -1 & 1 & -1 & 1 \\ 1 & -1 & 1 & -1 \\ -1 & 1 & -1 & 1 \end{bmatrix}$.

From Theorem 1.5-1, the designs that have $Z_2C_d^*$ symmetric have residual treatment effects orthogonal to direct treatment effects and the direct by residual treatment interaction.

d_1:

1 1 2 2
1 2 1 2
1 1 2 2
2 2 1 1
2 2 1 1
2 1 2 1

$$C_d^* = \begin{bmatrix} 3.0833 & -0.0833 & -0.6667 & -2.3333 \\ -0.0833 & 3.0833 & -2.3333 & -0.6667 \\ -0.6667 & -2.3333 & 3.0833 & -0.0833 \\ -2.3333 & -0.6667 & -0.0833 & 3.0833 \end{bmatrix}$$

$Z_1C_d^* = 3\ A$

$Z_2C_d^* = 2.4167\ B$

d_2:

1 1 2 2
1 2 1 2
1 2 1 2
2 1 2 1
2 2 1 1
2 1 2 1

$$C_d^* = \begin{bmatrix} 3.0833 & -0.0833 & 0.6667 & -2.3333 \\ -0.0833 & 3.0833 & -2.3333 & -0.6667 \\ -0.6667 & -2.3333 & 3.0833 & -0.0833 \\ -2.3333 & -0.6667 & -0.0833 & 3.0833 \end{bmatrix}$$

$Z_1C_d^* = 3\ A$

$Z_2C_d^* = 2.4167\ B$

d_3:

1 1 2 2
1 1 2 2
2 2 1 1
1 2 1 2
2 2 1 1
2 1 2 1

$$C_d^* = \begin{bmatrix} 3.4167 & -0.4167 & -1.0000 & -2.0000 \\ -0.4167 & 3.4167 & -2.0000 & -1.0000 \\ -1.0000 & -2.0000 & 3.4167 & -0.4167 \\ -2.0000 & -1.0000 & -0.4167 & 3.4167 \end{bmatrix}$$

$Z_1C_d^* = 3\ A$

$Z_2C_d^* = 2.4167\ B$

d_4:

1 1 2 2
1 2 1 2
2 2 1 1
1 2 1 2
2 1 2 1
2 1 2 1

$$C_d^* = \begin{bmatrix} 3.4167 & -0.4167 & -1.0000 & -2.0000 \\ -0.4167 & 3.4167 & -2.0000 & -1.0000 \\ -1.0000 & -2.0000 & 3.4167 & -0.4167 \\ -2.0000 & -1.0000 & -0.4167 & 3.4167 \end{bmatrix}$$

$Z_1C_d^* = 3\ A$

$Z_2C_d^* = 2.4167\ B$

d_5:

1 1 2 2
1 1 2 2
2 2 1 1
2 2 1 1
1 2 1 2
2 1 2 1

$$C_d^* = \begin{bmatrix} 2.9167 & 0.0833 & -0.5000 & -2.5000 \\ 0.0833 & 2.9167 & -2.5000 & -0.5000 \\ -0.5000 & -2.5000 & 2.9167 & 0.0833 \\ -2.5000 & -0.5000 & 0.0833 & 2.9167 \end{bmatrix}$$

$Z_1C_d^* = 3\ A$

$Z_2C_d^* = 2.4167\ B$

d_6:

1 1 2 2
1 2 1 2
2 2 1 1
2 2 1 1
1 1 2 2
2 1 2 1

$$C_d^* = \begin{bmatrix} 3.4167 & -0.4167 & -1.0000 & -2.0000 \\ -0.4167 & 3.4167 & -2.0000 & -1.0000 \\ -1.0000 & -2.0000 & 3.4167 & -0.4167 \\ -2.0000 & -1.0000 & -0.4167 & 3.4167 \end{bmatrix}$$

$Z_1C_d^* = 3$ A

$Z_2C_d^* = 2.4167$ B

d_7:

1 1 2 2
1 2 1 2
2 1 2 1
2 1 2 1
2 2 1 1
1 2 1 2

$$C_d^* = \begin{bmatrix} 3.4167 & -0.4167 & -1.0000 & -2.0000 \\ -0.4167 & 3.4167 & -2.0000 & -1.0000 \\ -1.0000 & -2.0000 & 3.4167 & -0.4167 \\ -2.0000 & -1.0000 & -0.4167 & 3.4167 \end{bmatrix}$$

$Z_1C_d^* = 3$ A

$Z_2C_d^* = 2.4167$ B

d_8:

1 1 2 2
1 2 1 2
2 2 1 1
2 1 2 1
2 1 2 1
1 2 1 2

$$C_d^* = \begin{bmatrix} 3.4167 & 0.4167 & -1.0000 & -2.0000 \\ 0.4167 & 3.4167 & -2.0000 & -1.0000 \\ 1.0000 & -2.0000 & 3.4167 & -0.4167 \\ 2.0000 & -1.0000 & -0.4167 & 3.4167 \end{bmatrix}$$

$Z_1C_d^* = 3$ A

$Z_2C_d^* = 2.4167$ B

d_9:

1 1 2 2
2 2 1 1
1 2 1 2
1 2 1 2
2 1 2 1
2 1 2 1

$$C_d^* = \begin{bmatrix} 2.9167 & 0.0833 & -0.5000 & -2.5000 \\ 0.0833 & 2.9167 & -2.5000 & -0.5000 \\ -0.5000 & -2.5000 & 2.9167 & 0.0833 \\ -2.5000 & -0.5000 & 0.0833 & 2.9167 \end{bmatrix}$$

$Z_1C_d^* = 3$ A

$Z_2C_d^* = 2.4167$ B

d_{10}:

1 1 2 2
2 2 1 1
2 2 1 1
1 2 1 2
1 1 2 2
2 1 2 1

$$C_d^* = \begin{bmatrix} 3.4167 & -0.4167 & -1.0000 & -2.0000 \\ -0.4167 & 3.4167 & -2.0000 & -1.0000 \\ -1.0000 & -2.0000 & 3.4167 & -0.4167 \\ -2.0000 & -1.0000 & -0.4167 & 3.4167 \end{bmatrix}$$

$Z_1C_d^* = 3$ A

$Z_2C_d^* = 2.4167$ B

d_{11}:

1 1 2 2
1 2 1 2
1 2 2 1
2 1 2 1
2 1 1 2
2 2 1 1

$$C_d^* = \begin{bmatrix} 3.7500 & -0.7500 & -1.4167 & -1.5833 \\ -0.7500 & 3.7500 & -1.5833 & -1.4167 \\ -1.4167 & -1.5833 & 3.9167 & -0.9167 \\ -1.5833 & -1.4167 & -0.9167 & 3.9167 \end{bmatrix}$$

$$Z_2C_d^* = \begin{bmatrix} 2.3333 & -2.3333 & 2.3333 & -2.3333 \\ -2.3333 & 2.3333 & 2.3333 & 2.3333 \\ 2.5000 & -2.5000 & 2.5000 & -2.5000 \\ -2.5000 & 2.5000 & -2.5000 & 2.5000 \end{bmatrix}$$

$Z_1C_d^* = 3$ A

d_{12}:

1 1 2 2
1 2 1 2
1 2 2 1
2 1 2 1
2 2 1 1
2 1 1 2

$$C_d^* = \begin{bmatrix} 3.5833 & -0.5833 & -1.3333 & -1.6667 \\ -0.5833 & 3.5833 & -1.6667 & -1.3333 \\ -1.3333 & -1.6667 & 3.9167 & -0.9167 \\ -1.6667 & -1.3333 & -0.9167 & 3.9167 \end{bmatrix}$$

$$Z_2C_d^* = \begin{bmatrix} 2.2500 & -2.2500 & 2.2500 & -2.2500 \\ -2.2500 & 2.2500 & -2.2500 & 2.2500 \\ 2.5833 & -2.5833 & 2.5833 & -2.5833 \\ -2.5833 & 2.5833 & -2.5833 & 2.5833 \end{bmatrix}$$

$Z_1C_d^* = 3$ A

d_{13}:

1 1 2 2
1 2 1 2
1 2 2 1
2 2 1 1
2 1 1 2
2 1 2 1

$$C_d^* = \begin{bmatrix} 3.7500 & -0.7500 & -1.3333 & -1.6667 \\ -0.7500 & 3.7500 & -1.6667 & -1.3333 \\ -1.3333 & -1.6667 & 3.7500 & -0.7500 \\ -1.6667 & -1.3333 & -0.7500 & 3.7500 \end{bmatrix}$$

$Z_1C_d^* = 3\ A$

$Z_2C_d^* = 2.4167\ B$

d_{14}:

1 1 2 2
1 2 1 2
1 2 2 1
2 2 1 1
2 1 2 1
2 1 1 2

$$C_d^* = \begin{bmatrix} 3.4167 & -0.4167 & -1.1667 & -1.8333 \\ -0.4167 & 3.4167 & -1.8333 & -1.1667 \\ 1.1667 & -1.8333 & 3.7500 & -0.7500 \\ -1.8333 & -1.1667 & -0.7500 & 3.7500 \end{bmatrix}$$

$$Z_2C_d^* = \begin{bmatrix} 2.2500 & -2.2500 & 2.2500 & -2.2500 \\ -2.2500 & 2.2500 & -2.2500 & 2.2500 \\ 2.5833 & -2.5833 & 2.5833 & -2.5833 \\ -2.5833 & 2.5833 & -2.5833 & 2.5833 \end{bmatrix}$$

$Z_1C_d^* = 3\ A$

d_{15}:

1 1 2 2
1 2 1 2
2 2 1 1
1 2 2 1
2 1 2 1
2 1 1 2

$$C_d^* = \begin{bmatrix} 3.9167 & -0.9167 & -1.5000 & -1.5000 \\ -0.9167 & 3.9167 & -1.5000 & -1.5000 \\ -1.5000 & -1.5000 & 3.9167 & -0.9167 \\ -1.5000 & -1.5000 & -0.9167 & 3.9167 \end{bmatrix}$$

$Z_1C_d^* = 3\ A$

$Z_2C_d^* = 2.4167\ B$

Appendix I: Linear Equations and the General Solution for SBURMDs(3,9s,6)

a) The system of linear equations

Using the method of Section 3.1 and 3.2 for SBURMDs with t=2, we can set up linear equations of the form $A\mathbf{x} = \mathbf{b}$ from the 90 possible sequences in Section 4.1 for t=3 and p=6. Here, $\mathbf{x} = (x_1, x_2, ..., x_{90})^T$, $\mathbf{b} = (5s, 5s, 5s, 5s, 5s, 5s, 5s, 5s, 5s, 3s, 3s, ..., 3s)^T$, and A is the 21 x 90 matrix of the coefficients of x_i given on the next page, with rank(A) = 15. Note, only the rows of A denoted by * are considered in any further calculations, as the resulting matrix has full row rank.

b) General Solution

Using the particular solution

$$\begin{cases} x_i = 1s & \text{for } i = 1, 2, 3, 46, 47, 48, 73, 74, 75, \quad s = 1, 2, 3, \ldots \\ x_i = 0 & \text{elsewhere,} \end{cases}$$

which is Patterson's 1970 design (1) in Table 2.2-5, and the kernel of A from part a), we get the following general solution for SBURMDs(3,9s,6)

$$\begin{bmatrix} x_1 \\ x_2 \\ x_3 \\ x_4 \\ x_5 \\ x_7 \\ x_8 \\ x_9 \\ x_{10} \\ x_{11} \\ x_{13} \\ x_{14} \\ x_{19} \\ x_{20} \end{bmatrix} = \frac{1}{4} K \cdot \begin{bmatrix} x_{12} \\ x_{15} \\ x_{16} \\ x_{17} \\ x_{18} \\ x_{21} \\ x_{22} \\ x_{23} \\ \cdot \\ \cdot \\ x_{45} \\ x_{46}-s \\ x_{47}-s \\ x_{48}-s \\ x_{49} \\ \cdot \\ \cdot \\ x_{72} \\ x_{73}-s \\ x_{74}-s \\ x_{75}-s \\ x_{76} \\ \cdot \\ \cdot \\ x_{90} \end{bmatrix},$$

where $0 \le x_{12}, x_{15}, x_{16}, x_{17}, x_{18}, x_{21}, x_{22}, x_{23}, \ldots, x_{90} \le 3s$, s=1,2,3,..., and K is given on page 73.

$$A = \begin{bmatrix} A_1 \\ A_2 \\ A_3 \end{bmatrix},$$

where A_1 is the matrix of the coefficients associated with the condition of strong balance, A_2 is the matrix of the coefficients when uniformity in rows with treatment 1, and A_3 is similarly associated with uniformity and treatment 2.

$A_1 =$

```
*[111111100100110101010001000000010001011011000000000000000101000000000010100110110000000010001]
*[101000102001101001201010101111100111100110212000111101111100101111100021111100011200110101 1]
 [000110010120010110001210111110111100101100000221110111100111111111021100000011101012101111 0]
*[000011001012001011100021111011111010110010000122011111010111111011121000000111001112101011]
*[111111010010011110001100000000001100101101000000000000010000100000010000110110100000000011 00]
 [110000210100110100120001110111010111010011221000111111011101011011100012111100021110011010 1]
*[011000021010011010012100011111001111001101122000111011111100101111110001121111000121010011 10]
*[000101100201100101010210111011110010110010002121011110011111111101112000000111100211110101]
 [111111001001101011100010000000100010110110000000000000010100000000001010011011000000001000 10]
```

$A_2 =$

```
*[100100100100100100100100100100100100100100100100100100100100100100100100100100100100100100]
*[100100100100100100001010001010001010001010001010001010001010001010001010001010001010001010]
*[001010001010001010100100100100100100100001010010001010001010001010001010001010001010001010]
*[001010010001010001001010010001010001100100100100100100100010001000100101000101001000100101]
*[010001001010010001010001001010010001010001001010010001100100100100100100010001010001001010]
 [010001010001001010010001010001001010010001010001001010010001010001010001100100100100100100]
```

$A_3 =$

```
*[010010010010010010010010010010010010010010010010010010010010010010010010010010010010010010]
*[010010010010010010100001100001100001100001100001100001100001100001100001100001001100100001]
*[100001100001100001010010010010010010010100001001100001100100001001100100001100001001100001]
*[100001001100001100100001001100001100010010010010010010001100100001100001001100100001001100]
 [001100100001001100001100100001001100001100100001001100010010010010010010001100001100100001]
 [001100001100100001001100001100100001001100001100100001001100001100001100010010010010010010]
```

$$K = \begin{bmatrix}
4 & -1 & -2 & 0 & 3 & 0 & 0 & 0 & 4 & 3 & 1 & 1 & -1 & -1 & 5 & 3 & 1 & 0 & -3 & -1 & 4 & 1 & 0 & 0 & 0 & -3 & 2 & 2 & -3 & 0 & 3 & 0 & 6 & 3 & -2 & 2 & 2 & -1 & 4 & 0 & 1 & -1 & 1 & 0 & 3 & 2 & 1 & 2 & 1 & 0 & 2 & -1 & 2 & 5 & 2 & -1 & -3 & 0 & 0 & -3 & 0 & 0 & 3 & 1 & -1 & 1 & 3 & 1 & 3 & 4 & 0 & -2 & -2 & 0 & 4 \\
4 & -1 & 0 & -2 & 3 & 0 & 4 & 4 & -4 & 1 & 5 & -1 & 3 & 1 & -1 & 1 & 5 & -2 & 3 & -1 & -2 & 5 & 0 & -4 & 6 & -3 & -4 & 2 & -1 & -2 & 9 & 2 & -2 & 3 & 2 & -2 & 8 & -1 & -2 & 2 & 3 & -5 & 5 & -2 & 1 & 2 & 1 & 2 & 5 & 2 & -4 & 7 & 0 & -1 & 0 & 1 & -3 & 0 & 2 & -5 & 4 & -2 & 1 & -1 & 1 & 1 & 5 & 3 & -1 & 0 & 2 & 0 & 4 & 0 & -2 \\
4 & -1 & 0 & 0 & 1 & 0 & -4 & 8 & 0 & -1 & 3 & 3 & -3 & 5 & 1 & -1 & 3 & 2 & -3 & 5 & -2 & 1 & 4 & -4 & 0 & 3 & -4 & 0 & -1 & 0 & 1 & 8 & 0 & -1 & 2 & 2 & 2 & 5 & -2 & -2 & 5 & -3 & 3 & 2 & -1 & 2 & 1 & 2 & -1 & 6 & -2 & 1 & 8 & -3 & 0 & -1 & -1 & -2 & 2 & -3 & 2 & 2 & -1 & -1 & -1 & 3 & 1 & 5 & 1 & 2 & -2 & 2 & -2 & 6 & -2 \\
-4 & -1 & -2 & 0 & -1 & 0 & -4 & -4 & 4 & -1 & -3 & 1 & -1 & -1 & 1 & -1 & -3 & 0 & -3 & -1 & 4 & -3 & -4 & 4 & -8 & 1 & 6 & -2 & 1 & 4 & -5 & -4 & 2 & -1 & -2 & 2 & -6 & -1 & 4 & 0 & -7 & 7 & -7 & 0 & 3 & -2 & -3 & 2 & -3 & -4 & 6 & -5 & -6 & 5 & -2 & -1 & 5 & 0 & -4 & 5 & -8 & 0 & 3 & 1 & -1 & 1 & -5 & -3 & 3 & -4 & 0 & 2 & -2 & -4 & 4 \\
-4 & -1 & 0 & -2 & -1 & 0 & 4 & -8 & 0 & 1 & -3 & -1 & 3 & -3 & -1 & 1 & -3 & -2 & 3 & -5 & 2 & 1 & -4 & 0 & 2 & -7 & 4 & 2 & -1 & 2 & 1 & -6 & -2 & 3 & -2 & -2 & 0 & -5 & 2 & 6 & -5 & -1 & 1 & -6 & 1 & 2 & -3 & -2 & 5 & -6 & 0 & 3 & -8 & -1 & 4 & -3 & 1 & 4 & -2 & -1 & 0 & -6 & 1 & 3 & 1 & -3 & 1 & -5 & -1 & 0 & -2 & 0 & 4 & -4 & -2 \\
-4 & -1 & 0 & 0 & -3 & 0 & 0 & 0 & -4 & -1 & -1 & -1 & 1 & 1 & -3 & -1 & -1 & -2 & 1 & 1 & -2 & -3 & 0 & 0 & 0 & 3 & -4 & 0 & 3 & 0 & -3 & 0 & -4 & -1 & 2 & -2 & -2 & 1 & -2 & -2 & 1 & 1 & -1 & 2 & -5 & -2 & 1 & -2 & -1 & 2 & -2 & -3 & 0 & -3 & 0 & 3 & -1 & -2 & 2 & 1 & -2 & 2 & -5 & -1 & 3 & -1 & -3 & 1 & -3 & -2 & 2 & -2 & 2 & -2 \\
-4 & -2 & -2 & 0 & 0 & -4 & 4 & -4 & -4 & -2 & 0 & -4 & 4 & -4 & -6 & 2 & 0 & -6 & 2 & -4 & -2 & 2 & 0 & -4 & 4 & -4 & -2 & -2 & 0 & -4 & 4 & -4 & -6 & 2 & 0 & -8 & 0 & -4 & -2 & 2 & -2 & -4 & 4 & -6 & -2 & 0 & -2 & -4 & 4 & -6 & -4 & 4 & -6 & -2 & 2 & -2 & -4 & 2 & 2 & -6 & 2 & -2 & -2 & 0 & 2 & -8 & 0 & -2 & -4 & -2 & 2 & -4 & 4 & -2 & -6 \\
-4 & -2 & 0 & -2 & 0 & -4 & 0 & -4 & 0 & 0 & -4 & -2 & 0 & -2 & -4 & 0 & 0 & -4 & 0 & -4 & 0 & -2 & 0 & 0 & -2 & 0 & 0 & -2 & -2 & -2 & -2 & -2 & -2 & -2 & 0 & -4 & -2 & -4 & 0 & 0 & -4 & 0 & 0 & 0 & -4 & 0 & -2 & -4 & 0 & -4 & -2 & 0 & -4 & 0 & 0 & 0 & -4 & -2 & 0 & 0 & -2 & 0 & 0 & -2 & 0 & -4 & -2 & -4 & 0 & -2 & 0 & -2 & -2 & -2 & 0 \\
-4 & -2 & 0 & 0 & -2 & -4 & 4 & -8 & 0 & 2 & -2 & -6 & 2 & -6 & -2 & 2 & -2 & -4 & 2 & -6 & 0 & 2 & -4 & 0 & 0 & -6 & 4 & 0 & -2 & -4 & 2 & -8 & 0 & 2 & -4 & -4 & 0 & -6 & 0 & 4 & -6 & -2 & -2 & -4 & 2 & 0 & -2 & -4 & 2 & -8 & 0 & 2 & -8 & 2 & 0 & -2 & -2 & 4 & -4 & 2 & 0 & -4 & 2 & 2 & -2 & -6 & 2 & -6 & -2 & 0 & 0 & -4 & 4 & -8 & 0 \\
4 & 0 & -2 & 0 & 2 & 0 & 0 & 4 & -4 & 0 & 2 & -2 & -2 & 2 & 0 & 0 & 2 & -2 & 0 & 2 & -2 & 4 & 0 & -4 & 4 & -2 & -2 & 2 & -2 & 0 & 2 & 0 & -2 & 0 & 0 & 0 & 4 & -2 & -2 & 2 & 4 & -6 & 2 & -2 & 0 & 0 & 0 & 0 & 2 & 2 & -4 & 2 & 2 & -4 & 2 & 0 & -2 & 2 & 2 & -4 & 2 & -2 & 0 & -2 & 0 & 2 & 2 & 0 & -2 & 2 & -2 & 0 & 0 & 2 & -2 \\
4 & 0 & 0 & -2 & 2 & 0 & -4 & 4 & 0 & -2 & 2 & 0 & -2 & 0 & 2 & -2 & 2 & 0 & -2 & 2 & 0 & 0 & 4 & -4 & 2 & 2 & -4 & 2 & 0 & -2 & 0 & 2 & -2 & 0 & 0 & 0 & 2 & 2 & -4 & -4 & 6 & -2 & 2 & 0 & -2 & 0 & 0 & 0 & -2 & 4 & -2 & -2 & 4 & -2 & 0 & 2 & -2 & -2 & 4 & -2 & 2 & 0 & -2 & 0 & -2 & 2 & 0 & 2 & -2 & 2 & 0 & -2 & -2 & 2 & 0 \\
0 & 4 & 4 & 0 & -4 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -4 & 0 & 4 & 4 & 0 & -4 & -4 & 4 & 0 & 0 & 4 & -4 & 0 & 4 & -4 & -4 & 4 & 0 & -4 & 4 & 0 & 0 & 4 & -4 & -4 & 4 & 0 & 0 & 4 & -4 & 0 & 4 & -4 & -4 & 4 & 0 & 0 & 4 & -4 & 0 & 4 & -4 & -4 & 4 & 0 & 0 & 4 & -4 & -4 & 4 & 0 & -4 & 0 & 4 & 4 & 0 & -4 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 4 & 0 & 4 & -4 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -4 & 4 & 0 & 4 & -4 & -4 & 0 & 4 & -4 & 4 & 0 & -4 & 0 & 4 & -4 & 0 & 4 & -4 & 4 & 0 & -4 & 0 & 4 & -4 & 4 & 0 & -4 & 0 & 4 & -4 & 4 & 0 & -4 & 0 & 4 & -4 & 4 & 0 & -4 & 0 & 4 & -4 & 4 & 0 & -4 & 0 & 4 & -4 & 4 & 0 & -4 & 0 & 4 & -4 & 4 & 0 & -4 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 4 & -4 & 4 & 0 & -4 & 0 & 4 & -4 & 4 & 0 & -4 & 0 & 4 & -4 & 4 & 0 & -4 & 0 & 4 & -4 & 4 & 0 & -4 & 0 & 4 & -4 & 4 & 0 & -4 & 0 & 4 & -4 & 4 & 0 & -4 & 0 & 4 & -4 & 4 & 0 & -4 & 0 & 4 & -4 & 4 & 0 & -4 & 0 & 4 & -4 & 4 & 0 & -4 & 0 & 4 & -4 & 4 & 0 & -4 & 0 & 4 & -4 & 4 & 0 & -4 & 0 & 4 & -4 & 4 & 0 \\
0 & 0 & 0 & 0 & 0 & 4 & -4 & 0 & 4 & 0 & -4 & 4 & -4 & 0 & 4 & 0 & -4 & 4 & -4 & 0 & 4 & 0 & -4 & 4 & -4 & 0 & 4 & 0 & -4 & 4 & -4 & 0 & 4 & 0 & -4 & 4 & -4 & 0 & 4 & 0 & -4 & 4 & -4 & 0 & 4 & 0 & -4 & 4 & -4 & 0 & 4 & 0 & -4 & 4 & -4 & 0 & 4 & 0 & -4 & 4 & -4 & 0 & 4 & 0 & -4 & 4 & -4 & 0 & 4 & 0 & -4 & 4 & -4 & 0 & 4
\end{bmatrix}$$

Appendix J: Finding Partially-Symmetric SBURMDs(3,9,6)

a) Input file **data4** representing the matrix A and the vector **b** from equation 4.1-1.

```
2 0 3 1 2 1 3 1 2 3 1 3 1 2 5 0 3 2 3 1 2 3 0 4 3 0 4 1 2 2
0 2 1 3 1 2 1 3 3 2 3 1 2 1 0 5 2 3 1 3 3 2 4 0 0 3 1 4 2 2
3 3 1 1 2 2 1 1 0 0 1 1 2 2 0 0 0 0 1 1 0 0 1 1 2 2 0 0 1 1
5 5 5
```

b) Pascal program **p6t3n9_psym.p** to find partially-symmetric SBURMDs(3,9,6).

```
{Written by Sandra Pattison 26/1/90}
{Program to find all partially-symmetric strongly balanced, uniform
RMD for   p=6,t=3,n=9}

program p6t2n9_psym(input,output,data4,p6t2n9_psym);

var     A:array[1..3,1..30] of integer;
        b:array[1..3]       of integer;
        x:array[1..30]      of integer;
        d:array[1..3]       of integer;
        i,j,k,q,r,ss,s        :integer;
        data4,p6t3n9_psym        :text;


procedure   Read_A;           {Reads in the matrix A from data4}
var   i,j   :integer;
begin       {Read_A}
for i:=1 to 3 do
   begin
      for j:= 1 to 30 do read(data4,A[i,j]);
      readln(data4);
   end;
end;        {Read_A}


procedure   Read_b;           {Reads in the vector b from data4}
var   i     :integer;
begin             {Read_b}
for i:=1 to 3 do
   begin
      read(data4,b[i]);
      b[i]:=b[i]*s;
   end;
end;        {Read_b}


procedure   Mult;             {calculates Ax=d}
var   i,j   :integer;
begin       {Mult}
for i:=1 to 3 do
   begin
      d[i]:=0;
      for j:=1 to 30 do d[i]:=d[i]+A[i,j]*x[j];
   end;
end;        {Mult}
```

```
procedure   Soln_Check;          {Checks to see if x is a solution to
                                  Ax=b, and if it is it's written to
                                  p6t3n9_psym.}
var   ss,q,r:integer;
begin       {Soln_Check}
Mult;
ss:=0;
for q:=1 to 3 do ss:=ss+(d[q]-b[q])*(d[q]-b[q]);
if ss=0 then
   begin
      for r:=1 to 30 do write(p6t3n9_psym,x[r]:3);
      writeln(p6t3n9_psym);
   end;
end;        {Soln_Check}



begin   {main program}
s:=1;
reset(data4);
rewrite(p6t3n9_psym);
Read_A;
Read_b;
for i:=1 to 30 do x[i]:=0;
for i:=1 to 30 do
   for j:= i to 30 do
       for k:=j to 30 do
         begin
            x[i]:=x[i]+1; x[j]:=x[j]+1; x[k]:=x[k]+1;
            Soln_Check;
            x[i]:=x[i]-1; x[j]:=x[j]-1;
         end;
end. {program}
```

c) Pascal program **p6t3n9_psymnoniso.p**, using the results of p6t3n9_psym.p to check for all partially-symmetric non-isomorphic SBURMDs(3,9,6).

```
{Written 19/6/90 by S.J. Pattison.
 Reading in all partially-symmetric p6t3n9 designs from p6t3n9_psym
 to find the non-isomorphic partially-symmetric solutions for p6t3n9
 and printing the results in p6t3n9_psymnoniso.
 This is achieved by checking, all the design in p6t3n9_psym to see
  if any of the design are the same once the the designs are permuted
  using (23).
 For example Patterson's (1970) design
            S1,1 S1,2 S1,3 S8,4 S8,5 S8,6 S13,1 S13,2 S13,3
 is the same as the design
            S1,4 S1,5 S1,6 S8,1 S8,2 S8,3 S13,4 S13,5 S13,6}

program
p6t3n9_psymnoniso(input,output,p6t3n9_psym,p6t3n9_psymnoniso);

type    design = array[1..15,1..2] of integer;
        dd     = array[1..102] of design;
        p      = array[1..1] of design;

var     d,try                              : design;
        d_read,d_noniso                    : dd;
        perm                               : p;
        i,j,k,count,iread,inoniso          : integer;
        new,match                          : boolean;
        p6t3n9_psym,p6t3n9_psymnoniso      : text;


procedure   read_design_array;      {Reads in all of the p6t3n9_psym
                                    designs into d_read.}
var   i,j,k : integer;
      begin       {read_design_array}
         for k := 1 to 102 do
            begin
               for i := 1 to 15 do
                  for j := 1 to 2 do
                     read(p6t3n9_psym,d[i,j]);
               readln(p6t3n9_psym);
               d_read[k] := d;
            end;
      end;        {read_design_array}


begin
   reset(p6t3n9_psym);
   rewrite(p6t3n9_psymnoniso);
   read_design_array;
   for i := 1 to 15 do
      for j := 1 to 2 do
         d_noniso[1][i,j] := d_read[1][i,j];
   count := 1;
   for iread := 2 to 102 do
     begin
        for i := 1 to 15 do
           for j := 1 to 2 do
              try[i,j] := d_read[iread][i,j];
```

```
        for i:= 1 to 15 do
            begin
               perm[1][i,2] := try[i,1]; perm[1][i,1] := try[i,2];
            end;
         new := true;
         inoniso := 1;
         while new and (inoniso <= count) do
            begin
               k := 0;
               repeat
                  k := k+1;
                  match := true;
                  for i := 1 to 15 do
                     for j:= 1 to 2 do
                        match := match and
                                 (perm[k][i,j]= d_noniso[inoniso][i,j]);
               until (k=1) or match;
               if (match = true) then  new := false
               else inoniso := inoniso+1;
            end;
         if (inoniso > count ) and new then
            begin
               count := count +1;
               for i := 1 to 15 do
                  for j := 1 to 2 do
                     d_noniso[count][i,j] := try[i,j];
            end;
      end;

      for inoniso := 1 to count do
         begin
            for i := 1 to 15 do
               for j:= 1 to 2 do
                  write(p6t3n9_psymnoniso,d_noniso[inoniso][i,j] :2);
            writeln(p6t3n9_psymnoniso);
         end;
end.
```

Appendix K: Non-Isomorphic, Partially-Symmetric SBURMDs(3,9,6)

The 51 partially-symmetric SBURMDs(3,9,6) from Section 4.1, where d_i* indicates those SBURMDs that have $Z_1C_d^*$ and $Z_2C_d^*$ symmetric from Section 1.5. Design d_{19} is Patterson's 1970 design and design d_{39} is Berenblut's 1964 design for t=3.

d_1

1	2	3	1	2	3	1	2	3
1	2	3	1	2	3	3	1	2
2	3	1	2	3	1	2	3	1
2	3	1	3	1	2	2	3	1
3	1	2	2	3	1	1	2	3
3	1	2	3	1	2	3	1	2

d_2

1	2	3	1	2	3	1	2	3
1	2	3	1	2	3	2	3	1
2	3	1	3	1	2	3	1	2
2	3	1	2	3	1	3	1	2
3	1	2	3	1	2	2	3	1
3	1	2	2	3	1	1	2	3

d_3*

1	2	3	1	2	3	1	2	3
1	2	3	1	2	3	3	1	2
2	3	1	3	1	2	2	3	1
2	3	1	2	3	1	2	3	1
3	1	2	3	1	2	3	1	2
3	1	2	2	3	1	1	2	3

d_4*

1	2	3	1	2	3	1	2	3
1	2	3	1	2	3	3	1	2
2	3	1	2	3	1	2	3	1
2	3	1	3	1	2	3	1	2
3	1	2	3	1	2	2	3	1
3	1	2	2	3	1	1	2	3

d_5

1	2	3	1	2	3	1	2	3
1	2	3	1	2	3	2	3	1
2	3	1	3	1	2	1	2	3
2	3	1	2	3	1	3	1	2
3	1	2	2	3	1	2	3	1
3	1	2	3	1	2	3	1	2

d_6

1	2	3	1	2	3	1	2	3
1	2	3	1	2	3	3	1	2
2	3	1	3	1	2	2	3	1
2	3	1	2	3	1	1	2	3
3	1	2	2	3	1	2	3	1
3	1	2	3	1	2	3	1	2

d_7

1	2	3	1	2	3	1	2	3
1	2	3	1	2	3	2	3	1
2	3	1	3	1	2	3	1	2
2	3	1	2	3	1	2	3	1
3	1	2	2	3	1	1	2	3
3	1	2	3	1	2	3	1	2

d_8

1	2	3	1	2	3	1	2	3
1	2	3	2	3	1	3	1	2
2	3	1	1	2	3	2	3	1
2	3	1	2	3	1	2	3	1
3	1	2	3	1	2	1	2	3
3	1	2	2	3	1	3	1	2

d_9

1	2	3	1	2	3	1	2	3
1	2	3	3	1	2	2	3	1
2	3	1	1	2	3	3	1	2
2	3	1	3	1	2	3	1	2
3	1	2	2	3	1	2	3	1
3	1	2	2	3	1	1	2	3

d_{10}

1	2	3	1	2	3	1	2	3
1	2	3	3	1	2	3	1	2
2	3	1	1	2	3	2	3	1
2	3	1	3	1	2	2	3	1
3	1	2	2	3	1	3	1	2
3	1	2	2	3	1	1	2	3

d_{11}

1	2	3	1	2	3	1	2	3
1	2	3	2	3	1	2	3	1
2	3	1	1	2	3	2	3	1
2	3	1	3	1	2	1	2	3
3	1	2	2	3	1	3	1	2
3	1	2	3	1	2	3	1	2

d_{12}*

1	2	3	1	2	3	1	2	3
1	2	3	3	1	2	3	1	2
2	3	1	1	2	3	3	1	2
2	3	1	2	3	1	2	3	1
3	1	2	3	1	2	2	3	1
3	1	2	2	3	1	1	2	3

d_{13}*

1	2	3	1	2	3	1	2	3
1	2	3	2	3	1	2	3	1
2	3	1	1	2	3	3	1	2
2	3	1	3	1	2	3	1	2
3	1	2	3	1	2	2	3	1
3	1	2	2	3	1	1	2	3

d_{14}

1	2	3	1	2	3	1	2	3
1	2	3	2	3	1	3	1	2
2	3	1	1	2	3	2	3	1
2	3	1	3	1	2	2	3	1
3	1	2	3	1	2	3	1	2
3	1	2	2	3	1	1	2	3

d_{15}

1	2	3	1	2	3	1	2	3
1	2	3	3	1	2	3	1	2
2	3	1	1	2	3	2	3	1
2	3	1	2	3	1	2	3	1
3	1	2	2	3	1	1	2	3
3	1	2	3	1	2	3	1	2

d_{16}

1	2	3	1	2	3	1	2	3
1	2	3	2	3	1	3	1	2
2	3	1	2	3	1	2	3	1
2	3	1	1	2	3	1	2	3
3	1	2	3	1	2	2	3	1
3	1	2	3	1	2	3	1	2

d_{17}

1	2	3	1	2	3	1	2	3
1	2	3	2	3	1	2	3	1
2	3	1	2	3	1	3	1	2
2	3	1	1	2	3	2	3	1
3	1	2	3	1	2	1	2	3
3	1	2	3	1	2	3	1	2

d_{18}

1	2	3	1	2	3	1	2	3
1	2	3	3	1	2	3	1	2
2	3	1	3	1	2	2	3	1
2	3	1	1	2	3	3	1	2
3	1	2	2	3	1	2	3	1
3	1	2	2	3	1	1	2	3

d_{19}*

1	2	3	1	2	3	1	2	3
1	2	3	3	1	2	2	3	1
2	3	1	2	3	1	2	3	1
2	3	1	1	2	3	3	1	2
3	1	2	3	1	2	3	1	2
3	1	2	2	3	1	1	2	3

d_{20}

1	2	3	1	2	3	1	2	3
1	2	3	2	3	1	3	1	2
2	3	1	2	3	1	2	3	1
2	3	1	3	1	2	2	3	1
3	1	2	1	2	3	1	2	3
3	1	2	3	1	2	3	1	2

d_{21}*

1	2	3	1	2	3	1	2	3
1	2	3	3	1	2	2	3	1
2	3	1	3	1	2	3	1	2
2	3	1	2	3	1	3	1	2
3	1	2	1	2	3	2	3	1
3	1	2	2	3	1	1	2	3

d_{22}

1	2	3	1	2	3	1	2	3
1	2	3	3	1	2	3	1	2
2	3	1	3	1	2	2	3	1
2	3	1	2	3	1	2	3	1
3	1	2	1	2	3	3	1	2
3	1	2	2	3	1	1	2	3

d_{23}*

1	2	3	1	2	3	1	2	3
1	2	3	3	1	2	3	1	2
2	3	1	2	3	1	3	1	2
2	3	1	3	1	2	2	3	1
3	1	2	1	2	3	2	3	1
3	1	2	2	3	1	1	2	3

d_{24}*

1	2	3	1	2	3	1	2	3
1	2	3	3	1	2	2	3	1
3	1	2	2	3	1	2	3	1
3	1	2	1	2	3	3	1	2
2	3	1	2	3	1	3	1	2
2	3	1	3	1	2	1	2	3

d_{25}

1	2	3	1	2	3	1	2	3
1	2	3	1	2	3	3	1	2
2	3	1	2	3	1	3	1	2
3	1	2	3	1	2	2	3	1
2	3	1	3	1	2	2	3	1
3	1	2	2	3	1	1	2	3

d_{26}

1	2	3	1	1	2	2	3	3
1	2	3	1	1	2	2	3	3
2	3	1	3	3	1	1	2	2
3	1	2	2	2	3	3	1	1
2	3	1	2	2	3	3	1	1
3	1	2	3	3	1	1	2	2

d_{27}

1	2	3	1	2	3	1	2	3
1	2	3	1	2	3	2	3	1
2	3	1	3	1	2	2	3	1
3	1	2	2	3	1	1	2	3
2	3	1	2	3	1	3	1	2
3	1	2	3	1	2	3	1	2

d_{28}

1	2	3	1	1	2	2	3	3
1	2	3	2	2	3	3	1	1
2	3	1	2	2	3	3	1	1
3	1	2	1	1	2	2	3	3
2	3	1	3	3	1	1	2	2
3	1	2	3	3	1	1	2	2

d_{29}

1	2	3	1	2	3	1	2	3
1	2	3	3	1	2	3	1	2
2	3	1	3	1	2	3	1	2
3	1	2	1	2	3	2	3	1
2	3	1	2	3	1	2	3	1
3	1	2	2	3	1	1	2	3

d_{30}

1	1	2	2	3	3	1	2	3
1	1	2	2	3	3	3	1	2
2	2	3	3	1	1	1	2	3
3	3	1	1	2	2	3	1	2
3	3	1	1	2	2	2	3	1
2	2	3	3	1	1	2	3	1

d_{31}

1	1	2	2	3	3	1	2	3
1	1	2	2	3	3	2	3	1
2	2	3	3	1	1	1	2	3
3	3	1	1	2	2	3	1	2
3	3	1	1	2	2	3	1	2
2	2	3	3	1	1	2	3	1

d_{32}

1	1	2	2	3	3	1	2	3
1	1	2	2	3	3	3	1	2
2	2	3	3	1	1	3	1	2
3	3	1	1	2	2	2	3	1
3	3	1	1	2	2	1	2	3
2	2	3	3	1	1	2	3	1

d_{33}

1	2	3	1	2	3	1	2	3
1	2	3	1	2	3	2	3	1
2	3	1	3	1	2	3	1	2
3	1	2	2	3	1	3	1	2
3	1	2	2	3	1	2	3	1
2	3	1	3	1	2	1	2	3

d_{34}*

1	2	3	1	2	3	1	2	3
1	2	3	2	3	1	3	1	2
2	3	1	1	2	3	3	1	2
3	1	2	2	3	1	2	3	1
3	1	2	3	1	2	2	3	1
2	3	1	3	1	2	1	2	3

d_{35}

1	2	3	1	2	3	1	2	3
1	2	3	3	1	2	3	1	2
2	3	1	1	2	3	3	1	2
3	1	2	3	1	2	1	2	3
3	1	2	2	3	1	2	3	1
2	3	1	2	3	1	2	3	1

d_{36}

1	2	3	1	2	3	1	2	3
1	2	3	2	3	1	3	1	2
2	3	1	1	2	3	3	1	2
3	1	2	3	1	2	1	2	3
3	1	2	3	1	2	2	3	1
2	3	1	2	3	1	2	3	1

d_{37}

1	2	3	1	2	3	1	2	3
1	2	3	3	1	2	3	1	2
2	3	1	1	2	3	3	1	2
3	1	2	2	3	1	2	3	1
3	1	2	2	3	1	2	3	1
2	3	1	3	1	2	1	2	3

d_{38}

1	2	3	1	2	3	1	2	3
1	2	3	2	3	1	2	3	1
2	3	1	2	3	1	3	1	2
3	1	2	1	2	3	3	1	2
3	1	2	3	1	2	2	3	1
2	3	1	3	1	2	1	2	3

d_{39}*

1	2	3	1	2	3	1	2	3
1	2	3	2	3	1	3	1	2
2	3	1	2	3	1	2	3	1
3	1	2	1	2	3	2	3	1
3	1	2	3	1	2	3	1	2
2	3	1	3	1	2	1	2	3

d_{40}

1	2	3	1	2	3	1	2	3
1	2	3	3	1	2	3	1	2
2	3	1	3	1	2	3	1	2
3	1	2	1	2	3	2	3	1
3	1	2	2	3	1	1	2	3
2	3	1	2	3	1	2	3	1

d_{41}

1	2	3	1	2	3	1	2	3
1	2	3	2	3	1	3	1	2
2	3	1	2	3	1	3	1	2
3	1	2	3	1	2	2	3	1
3	1	2	1	2	3	2	3	1
2	3	1	3	1	2	1	2	3

d_{42}

1	2	3	1	2	3	1	2	3
1	2	3	3	1	2	2	3	1
2	3	1	2	3	1	2	3	1
3	1	2	2	3	1	3	1	2
3	1	2	1	2	3	3	1	2
2	3	1	3	1	2	1	2	3

d_{43}

1	2	3	1	1	2	2	3	3
2	3	1	2	2	3	3	1	1
1	2	3	2	2	3	3	1	1
2	3	1	1	1	2	2	3	3
3	1	2	3	3	1	1	2	2
3	1	2	3	3	1	1	2	2

d_{44}

1	2	3	1	2	3	1	2	3
2	3	1	3	1	2	3	1	2
1	2	3	3	1	2	3	1	2
2	3	1	1	2	3	2	3	1
3	1	2	2	3	1	2	3	1
3	1	2	2	3	1	1	2	3

d_{45}

1	2	3	1	1	2	2	3	3
3	1	2	2	2	3	3	1	1
1	2	3	2	2	3	3	1	1
2	3	1	1	1	2	2	3	3
2	3	1	3	3	1	1	2	2
3	1	2	3	3	1	1	2	2

d_{46}*

1	2	3	1	2	3	1	2	3
3	1	2	3	1	2	3	1	2
1	2	3	3	1	2	3	1	2
2	3	1	1	2	3	2	3	1
2	3	1	2	3	1	2	3	1
3	1	2	2	3	1	1	2	3

d_{47}

1	2	3	1	2	3	1	2	3
2	3	1	3	1	2	2	3	1
2	3	1	3	1	2	3	1	2
1	2	3	1	2	3	3	1	2
3	1	2	2	3	1	2	3	1
3	1	2	2	3	1	1	2	3

d_{48}

1	1	2	2	3	3	1	2	3
3	3	1	1	2	2	3	1	2
3	3	1	1	2	2	3	1	2
1	1	2	2	3	3	2	3	1
2	2	3	3	1	1	1	2	3
2	2	3	3	1	1	2	3	1

d_{49}*

1	2	3	1	2	3	1	2	3
3	1	2	2	3	1	3	1	2
3	1	2	2	3	1	3	1	2
1	2	3	3	1	2	2	3	1
2	3	1	1	2	3	2	3	1
2	3	1	3	1	2	1	2	3

d_{50}*

1	2	3	1	2	3	1	2	3
3	1	2	3	1	2	2	3	1
3	1	2	2	3	1	2	3	1
1	2	3	2	3	1	3	1	2
2	3	1	1	2	3	3	1	2
2	3	1	3	1	2	1	2	3

d_{51}

1	2	3	1	2	3	1	2	3
2	3	1	3	1	2	2	3	1
2	3	1	3	1	2	3	1	2
3	1	2	2	3	1	3	1	2
3	1	2	2	3	1	2	3	1
1	2	3	1	2	3	1	2	3

Appendix L: Symmetric SBURMDs(3,18,6)

The 72 solutions to Equation (4.1-2), where sx_i, i=1,2,...,15, represents the number of times sequences of type $S_{i,1}$ are present in the design and hence the number of times the other 5 sequences in the permutation group are present. The sequences $S_{i,j}$ are given in Table 4.1-1.

	sx_i : i=														
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
	1	2	0	0	0	0	0	0	0	0	0	0	0	0	0
	1	1	0	1	0	0	0	0	0	0	0	0	0	0	0
	1	1	0	0	0	1	0	0	0	0	0	0	0	0	0
	1	1	0	0	0	0	0	0	0	1	0	0	0	0	0
	1	1	0	0	0	0	0	0	0	0	0	1	0	0	0
*	1	1	0	0	0	0	0	0	0	0	0	0	0	0	1
	1	0	1	0	1	0	0	0	0	0	0	0	0	0	0
	1	0	1	0	0	0	0	1	0	0	0	0	0	0	0
	1	0	1	0	0	0	0	0	1	0	0	0	0	0	0
	1	0	1	0	0	0	0	0	0	1	0	0	0	0	0
*	1	0	1	0	0	0	0	0	0	0	0	0	0	1	0
	1	0	0	2	0	0	0	0	0	0	0	0	0	0	0
	1	0	0	1	0	1	0	0	0	0	0	0	0	0	0
	1	0	0	1	0	0	0	0	0	1	0	0	0	0	0
	1	0	0	1	0	0	0	0	0	0	0	1	0	0	0
	1	0	0	1	0	0	0	0	0	0	0	0	0	0	1
	1	0	0	0	1	0	1	0	0	0	0	0	0	0	0
*	1	0	0	0	1	0	0	0	0	0	0	0	1	0	0
	1	0	0	0	0	2	0	0	0	0	0	0	0	0	0
	1	0	0	0	0	1	0	0	0	1	0	0	0	0	0
	1	0	0	0	0	1	0	0	0	0	0	1	0	0	0
*	1	0	0	0	0	1	0	0	0	0	0	0	0	0	1
	1	0	0	0	0	0	1	1	0	0	0	0	0	0	0
	1	0	0	0	0	0	1	0	1	0	0	0	0	0	0
	1	0	0	0	0	0	1	0	0	0	1	0	0	0	0
	1	0	0	0	0	0	1	0	0	0	0	0	0	1	0
*	1	0	0	0	0	0	0	1	0	0	0	0	1	0	0
*	1	0	0	0	0	0	0	0	1	0	0	0	1	0	0
	1	0	0	0	0	0	0	0	0	2	0	0	0	0	0
	1	0	0	0	0	0	0	0	0	1	0	1	0	0	0
*	1	0	0	0	0	0	0	0	0	1	0	0	0	0	1
*	1	0	0	0	0	0	0	0	0	0	1	0	1	0	0
	1	0	0	0	0	0	0	0	0	0	0	2	0	0	0
*	1	0	0	0	0	0	0	0	0	0	0	1	0	0	1
	1	0	0	0	0	0	0	0	0	0	0	0	1	1	0
	1	0	0	0	0	0	0	0	0	0	0	0	0	2	0

	sx_i : i=														
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
	0	1	2	0	0	0	0	0	0	0	0	0	0	0	0
	0	1	1	0	0	0	1	0	0	0	0	0	0	0	0
	0	1	1	0	0	0	0	0	0	0	0	0	1	0	0
	0	1	0	0	0	0	2	0	0	0	0	0	0	0	0
*	0	1	0	0	0	0	1	0	0	0	0	0	1	0	0
	0	1	0	0	0	0	0	0	0	0	0	0	2	0	0
	0	0	2	1	0	0	0	0	0	0	0	0	0	0	0
	0	0	2	0	0	1	0	0	0	0	0	0	0	0	0
	0	0	2	0	0	0	0	0	0	1	0	0	0	0	0
	0	0	2	0	0	0	0	0	0	0	0	1	0	0	0
	0	0	2	0	0	0	0	0	0	0	0	0	0	0	1
	0	0	1	1	0	0	1	0	0	0	0	0	0	0	0
*	0	0	1	1	0	0	0	0	0	0	0	0	1	0	0
	0	0	1	0	0	1	1	0	0	0	0	0	0	0	0
	0	0	1	0	0	1	0	0	0	0	0	0	1	0	0
	0	0	1	0	0	0	1	0	0	1	0	0	0	0	0
	0	0	1	0	0	0	1	0	0	0	0	1	0	0	0
*	0	0	1	0	0	0	1	0	0	0	0	0	0	0	1
	0	0	1	0	0	0	0	0	0	1	0	0	1	0	0
	0	0	1	0	0	0	0	0	0	0	0	0	0	1	0
	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1
	0	0	0	1	0	0	2	0	0	0	0	0	0	0	0
	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0
	0	0	0	0	1	0	0	0	0	0	1	2	0	0	0
*	0	0	0	0	0	1	1	0	0	0	0	0	1	0	0
	0	0	0	0	0	1	0	0	0	0	0	0	2	0	0
	0	0	0	0	0	0	2	0	0	1	0	0	0	0	0
	0	0	0	0	0	0	2	0	0	0	0	1	0	0	0
	0	0	0	0	0	0	2	0	0	0	0	0	0	0	1
*	0	0	0	0	0	0	1	0	0	1	0	0	1	0	0
*	0	0	0	0	0	0	1	0	0	0	0	0	1	1	0
	0	0	0	0	0	0	1	0	0	0	0	0	0	1	0
	0	0	0	0	0	0	0	0	0	1	0	0	2	0	0
	0	0	0	0	0	0	0	0	0	0	0	1	2	0	0
	0	0	0	0	0	0	0	0	0	0	0	0	2	0	1

* - Designs where $Z_2C_d^*$ is symmetric

Appendix M: Analysis of the Synthetic Octapeptide Example

a) MATLAB program to obtain the sums of squares for the analyses of variances I and II in Table 5.3-2, for 12 subjects and 8 subjects respectively.

```
//      Checking the ANOVA in Thorton et al, (1987)
//      Six Sequence carry-over design for the determination of the effect
//      of a drug in reducing food intake.
//      Using log(food intake) as y variate
//
//      Linear Model:
//      y= g.m + subject + period + direct + resid + error
//
//      Treatment Sequences: S S S S S S P P P P P P
//                           S S P P P P S S S S P P
//                           P P P P S S P P S S S S
//                           P P S S P P S S P P S S
X=[ 1  1  0  0  0  0  0  0  0  0  0  0  1  0  0  1  0
    1  1  0  0  0  0  0  0  0  0  0  0  0  1  0  1  1
    1  1  0  0  0  0  0  0  0  0  0  0  0  0  1 -1  1
    1  1  0  0  0  0  0  0  0  0  0  0 -1 -1 -1 -1 -1
    1  0  1  0  0  0  0  0  0  0  0  0  1  0  0  1  0
    1  0  1  0  0  0  0  0  0  0  0  0  0  1  0  1  1
    1  0  1  0  0  0  0  0  0  0  0  0  0  0  1 -1  1
    1  0  1  0  0  0  0  0  0  0  0  0 -1 -1 -1 -1 -1
    1  0  0  1  0  0  0  0  0  0  0  0  1  0  0  1  0
    1  0  0  1  0  0  0  0  0  0  0  0  0  1  0 -1  1
    1  0  0  1  0  0  0  0  0  0  0  0  0  0  1 -1 -1
    1  0  0  1  0  0  0  0  0  0  0  0 -1 -1 -1  1 -1
    1  0  0  0  1  0  0  0  0  0  0  0  1  0  0  1  0
    1  0  0  0  1  0  0  0  0  0  0  0  0  1  0 -1  1
    1  0  0  0  1  0  0  0  0  0  0  0  0  0  1 -1 -1
    1  0  0  0  1  0  0  0  0  0  0  0 -1 -1 -1  1 -1
    1  0  0  0  0  1  0  0  0  0  0  0  1  0  0  1  0
    1  0  0  0  0  1  0  0  0  0  0  0  0  1  0 -1  1
    1  0  0  0  0  1  0  0  0  0  0  0  0  0  1  1 -1
    1  0  0  0  0  1  0  0  0  0  0  0 -1 -1 -1 -1  1
    1  0  0  0  0  0  1  0  0  0  0  0  1  0  0  1  0
    1  0  0  0  0  0  1  0  0  0  0  0  0  1  0 -1  1
    1  0  0  0  0  0  1  0  0  0  0  0  0  0  1  1 -1
    1  0  0  0  0  0  1  0  0  0  0  0 -1 -1 -1 -1  1
    1  0  0  0  0  0  0  1  0  0  0  0  1  0  0 -1  0
    1  0  0  0  0  0  0  1  0  0  0  0  0  1  0  1 -1
    1  0  0  0  0  0  0  1  0  0  0  0  0  0  1 -1  1
    1  0  0  0  0  0  0  1  0  0  0  0 -1 -1 -1  1 -1
    1  0  0  0  0  0  0  0  1  0  0  0  1  0  0 -1  0
    1  0  0  0  0  0  0  0  1  0  0  0  0  1  0  1 -1
    1  0  0  0  0  0  0  0  1  0  0  0  0  0  1 -1  1
    1  0  0  0  0  0  0  0  1  0  0  0 -1 -1 -1  1 -1
    1  0  0  0  0  0  0  0  0  1  0  0  1  0  0 -1  0
    1  0  0  0  0  0  0  0  0  1  0  0  0  1  0  1 -1
    1  0  0  0  0  0  0  0  0  1  0  0  0  0  1  1  1
    1  0  0  0  0  0  0  0  0  1  0  0 -1 -1 -1 -1  1
    1  0  0  0  0  0  0  0  0  0  1  0  1  0  0 -1  0
    1  0  0  0  0  0  0  0  0  0  1  0  0  1  0  1 -1
    1  0  0  0  0  0  0  0  0  0  1  0 -1 -1 -1  1  1
    1  0  0  0  0  0  0  0  0  0  0  1  1  0  0 -1  0
    1  0  0  0  0  0  0  0  0  0  0  1  0  1  0 -1 -1
    1  0  0  0  0  0  0  0  0  0  0  1  0  0  1  1 -1
    1  0  0  0  0  0  0  0  0  0  0  1 -1 -1 -1  1  1
    1 -1 -1 -1 -1 -1 -1 -1 -1 -1 -1 -1  1  0  0 -1  0
    1 -1 -1 -1 -1 -1 -1 -1 -1 -1 -1 -1  0  1  0 -1 -1
    1 -1 -1 -1 -1 -1 -1 -1 -1 -1 -1 -1  0  0  1  1 -1
    1 -1 -1 -1 -1 -1 -1 -1 -1 -1 -1 -1 -1 -1 -1  1  1 ];
```

```
 y =[360 ;  416 ;  519 ;  584 ; 263 ; 139 ; 401 ; 431 ;
     715 ; 1130 ; 1319 ; 1483 ; 887 ; 882 ; 954 ; 582 ;
     558 ; 1427 ;  536 ; 1009 ; 531 ; 525 ; 472 ; 289 ;
     521 ;  466 ;  417 ;  255 ; 610 ; 471 ; 589 ; 690 ;
     659 ;  664 ;  663 ;  491 ; 517 ; 444 ; 362 ; 362 ;
     378 ;  449 ;  474 ;  500 ; 538 ; 449 ; 397 ; 192 ];

exec('Anova.mat')
y =   log(y);
y =   y- sum(y)/48*J(48,1);
X'*X
    48   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0
     0   8   4   4   4   4   4   4   4   4   4   4   0   0   0   0  -2
     0   4   8   4   4   4   4   4   4   4   4   4   0   0   0   0  -2
     0   4   4   8   4   4   4   4   4   4   4   4   0   0   0   0   0
     0   4   4   4   8   4   4   4   4   4   4   4   0   0   0   0   0
     0   4   4   4   4   8   4   4   4   4   4   4   0   0   0   0   0
     0   4   4   4   4   4   8   4   4   4   4   4   0   0   0   0   0
     0   4   4   4   4   4   4   8   4   4   4   4   0   0   0   0  -2
     0   4   4   4   4   4   4   4   8   4   4   4   0   0   0   0  -2
     0   4   4   4   4   4   4   4   4   8   4   4   0   0   0   0  -2
     0   4   4   4   4   4   4   4   4   4   8   4   0   0   0   0  -2
     0   4   4   4   4   4   4   4   4   4   4   8   0   0   0   0   0
     0   0   0   0   0   0   0   0   0   0   0   0  24  12  12   0   0
     0   0   0   0   0   0   0   0   0   0   0   0  12  24  12   0   0
     0   0   0   0   0   0   0   0   0   0   0   0  12  12  24   0   0
     0   0   0   0   0   0   0   0   0   0   0   0   0   0   0  48 -12
     0  -2  -2   0   0   0   0  -2  -2  -2  -2   0   0   0   0 -12  36

Bhat = inv(X'*X)*X'*y;      yhat = X*Bhat;       res = y-yhat;
TotSSq = y'*y;              RegSSq = y'*yhat;    ResSSq = TotSSq-RegSSq;

X1 = X(:,1:16);
Bhat1 = inv(X1'*X1)*X1'*y;  yhat1 = X1*Bhat1;
res1 = y-yhat1;             Reg1SSq = y'*yhat1;

X2a = X(:,1:15);            X2b = X(:,17);       X2 = [X2a X2b];
Bhat2 = inv(X2'*X2)*X2'*y;  yhat2 = X2*Bhat2;
res2 = y-yhat2;             Reg2SSq = y'*yhat2;

X3a = X(:,1:12);            X3b = X(:,16:17);    X3 = [X3a X3b];
Bhat3 = inv(X3'*X3)*X3'*y;  yhat3 = X3*Bhat3;
res3 = y-yhat3;             Reg3SSq = y'*yhat3;

X4a=X(:,1);                 X4b = X(:,13:17);    X4 = [X4a X4b];
Bhat4 = inv(X4'*X4)*X4'*y;  yhat4 = X4*Bhat4;
res4 = y-yhat4;             Reg4SSq = y'*yhat4;

CO =     RegS-Reg1;
DIR =    RegS-Reg2;
PERIOD = RegS-Reg3;
SUBJ =   RegS-Reg4;
check =  CO+DIR+PERIOD+SUBJ ;

 TotSSq  =   10.3246
 RegSSq  =    7.7706
 ResSSq  =    2.5541
 CO      =    0.2477
 DIR     =    0.8288
 PERI    =    0.0860
 SUBJ    =    6.6091
 check   =    7.7715
```

```
//      ++++++++++++++++++++++++++++++++++++++++++++++++++++++++++++++++++++
//      Using Sequences 1,2,5 and 6, which make up a SBURMD.
//      The y variate corresponds to these sequences and is again
//      log(food intake)
//
//      Linear Model:
//      y= g.m + subject + period + direct + resid + error
//
//      Treatment Sequences: S S S S P P P P
//                           S S P P S S P P
//                           P P P P S S S S
//                           P P S S P P S S

Z = [X(1:16,1:5) X(1:16,10:17)];
ZZ= [X(33:48,1:5) X(33:48,10:17)];
X = [ Z ; ZZ ];

y = [y(1:16,:) ; y(33:48,:)];

exec('Anova.mat');

X'*X
    32    0    0    0    0    0    0    0    0    0    0    0    0
     0    8    4    4    4    4    4    4    0    0    0    0    0
     0    4    8    4    4    4    4    4    0    0    0    0    0
     0    4    4    8    4    4    4    4    0    0    0    0    2
     0    4    4    4    8    4    4    4    0    0    0    0    2
     0    4    4    4    4    8    4    4    0    0    0    0    2
     0    4    4    4    4    4    8    4    0    0    0    0    2
     0    4    4    4    4    4    4    8    0    0    0    0    0
     0    0    0    0    0    0    0    0   16    8    8    0    0
     0    0    0    0    0    0    0    0    8   16    8    0    0
     0    0    0    0    0    0    0    0    8    8   16    0    0
     0    0    0    0    0    0    0    0    0    0    0   32    0
     0    0    0    2    2    2    2    0    0    0    0    0   24

 TotSSq  =7.8053
 RegSSq  =6.4607
 ResSSq  =1.3447
 CO      =0.3132
 DIR     =0.4398
 PERI    =0.1260
 SUBJ    =5.1839
 check   =6.0628
```

b) MATLAB program partitioning the subjects into sequences and subjects within sequences, for the analyses of variances I and II in Table 5.3-2, for 12 subjects and 8 subjects respectively.

```
//      Partitioning the 12 subjects into a sequence and subj within seq.
//      Linear Model:
//      log(y)= g.m + sequence + sequence(subj) + period + direct + resid
//
//      Treatment Sequences: S S S S S S P P P P P P
//                           S S P P P P S S S S P P
//                           P P P P S S P P S S S S
//                           P P S S P P S S P P S S
//
X=[1  1  0  0  0  0  1  0  0  0  0  0  1  0  0  1  0
   1  1  0  0  0  0  1  0  0  0  0  0  0  1  0 -1  1
   1  1  0  0  0  0  1  0  0  0  0  0  0  0  1 -1 -1
   1  1  0  0  0  0  1  0  0  0  0  0 -1 -1 -1  1 -1
   1  1  0  0  0  0 -1  0  0  0  0  0  1  0  0  1  0
   1  1  0  0  0  0 -1  0  0  0  0  0  0  1  0 -1  1
   1  1  0  0  0  0 -1  0  0  0  0  0  0  0  1 -1 -1
   1  1  0  0  0  0 -1  0  0  0  0  0 -1 -1 -1  1 -1
   1  0  1  0  0  0  0  1  0  0  0  0  1  0  0 -1  0
   1  0  1  0  0  0  0  1  0  0  0  0  0  1  0  1 -1
   1  0  1  0  0  0  0  1  0  0  0  0  0  0  1  1  1
   1  0  1  0  0  0  0  1  0  0  0  0 -1 -1 -1 -1  1
   1  0  1  0  0  0  0 -1  0  0  0  0  1  0  0 -1  0
   1  0  1  0  0  0  0 -1  0  0  0  0  0  1  0  1 -1
   1  0  1  0  0  0  0 -1  0  0  0  0  0  0  1  1  1
   1  0  1  0  0  0  0 -1  0  0  0  0 -1 -1 -1 -1  1
   1  0  0  1  0  0  0  0  1  0  0  0  1  0  0  1  0
   1  0  0  1  0  0  0  0  1  0  0  0  0  1  0  1  1
   1  0  0  1  0  0  0  0  1  0  0  0  0  0  1 -1  1
   1  0  0  1  0  0  0  0  1  0  0  0 -1 -1 -1 -1 -1
   1  0  0  1  0  0  0  0 -1  0  0  0  1  0  0  1  0
   1  0  0  1  0  0  0  0 -1  0  0  0  0  1  0  1  1
   1  0  0  1  0  0  0  0 -1  0  0  0  0  0  1 -1  1
   1  0  0  1  0  0  0  0 -1  0  0  0 -1 -1 -1 -1 -1
   1  0  0  0  1  0  0  0  0  1  0  0  1  0  0 -1  0
   1  0  0  0  1  0  0  0  0  1  0  0  0  1  0 -1 -1
   1  0  0  0  1  0  0  0  0  1  0  0  0  0  1  1 -1
   1  0  0  0  1  0  0  0  0  1  0  0 -1 -1 -1  1  1
   1  0  0  0  1  0  0  0  0 -1  0  0  1  0  0 -1  0
   1  0  0  0  1  0  0  0  0 -1  0  0  0  1  0 -1 -1
   1  0  0  0  1  0  0  0  0 -1  0  0  0  0  1  1 -1
   1  0  0  0  1  0  0  0  0 -1  0  0 -1 -1 -1  1  1
   1  0  0  0  0  1  0  0  0  0  1  0  1  0  0 -1  0
   1  0  0  0  0  1  0  0  0  0  1  0  0  1  0  1 -1
   1  0  0  0  0  1  0  0  0  0  1  0  0  0  1 -1  1
   1  0  0  0  0  1  0  0  0  0  1  0 -1 -1 -1  1 -1
   1  0  0  0  0  1  0  0  0  0 -1  0  1  0  0 -1  0
   1  0  0  0  0  1  0  0  0  0 -1  0  0  1  0  1 -1
   1  0  0  0  0  1  0  0  0  0 -1  0 -1 -1 -1  1 -1
   1 -1 -1 -1 -1 -1  0  0  0  0  0  1  1  0  0  1  0
   1 -1 -1 -1 -1 -1  0  0  0  0  0  1  0  1  0 -1  1
   1 -1 -1 -1 -1 -1  0  0  0  0  0  1  0  0  1  1 -1
   1 -1 -1 -1 -1 -1  0  0  0  0  0  1 -1 -1 -1 -1  1
   1 -1 -1 -1 -1 -1  0  0  0  0  0 -1  1  0  0  1  0
   1 -1 -1 -1 -1 -1  0  0  0  0  0 -1  0  1  0 -1  1
   1 -1 -1 -1 -1 -1  0  0  0  0  0 -1  0  0  1  1 -1
   1 -1 -1 -1 -1 -1  0  0  0  0  0 -1 -1 -1 -1 -1  1 ];
```

```
y =[ 360 ;  416 ;  519 ;  584 ; 263 ; 139 ; 401 ; 431 ;
     715 ; 1130 ; 1319 ; 1483 ; 887 ; 882 ; 954 ; 582 ;
     558 ; 1427 ;  536 ; 1009 ; 531 ; 525 ; 472 ; 289 ;
     521 ;  466 ;  417 ;  255 ; 610 ; 471 ; 589 ; 690 ;
     659 ;  664 ;  663 ;  491 ; 517 ; 444 ; 362 ; 362 ;
     378 ;  449 ;  474 ;  500 ; 538 ; 449 ; 397 ; 192 ];

exec('Anova1.mat');
X'*X
   48    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0
    0   16    8    8    8    8    0    0    0    0    0    0    0    0    0    0   -4
    0    8   16    8    8    8    0    0    0    0    0    0    0    0    0    0    0
    0    8    8   16    8    8    0    0    0    0    0    0    0    0    0    0    0
    0    8    8    8   16    8    0    0    0    0    0    0    0    0    0    0   -4
    0    8    8    8    8   16    0    0    0    0    0    0    0    0    0    0   -4
    0    0    0    0    0    0    8    0    0    0    0    0    0    0    0    0    0
    0    0    0    0    0    0    0    8    0    0    0    0    0    0    0    0    0
    0    0    0    0    0    0    0    0    8    0    0    0    0    0    0    0    0
    0    0    0    0    0    0    0    0    0    8    0    0    0    0    0    0    0
    0    0    0    0    0    0    0    0    0    0    8    0    0    0    0    0    0
    0    0    0    0    0    0    0    0    0    0    0    8    0    0    0    0    0
    0    0    0    0    0    0    0    0    0    0    0    0   24   12   12    0    0
    0    0    0    0    0    0    0    0    0    0    0    0   12   24   12    0    0
    0    0    0    0    0    0    0    0    0    0    0    0   12   12   24    0    0
    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0   48  -12
    0   -4    0    0   -4   -4    0    0    0    0    0    0    0    0    0  -12   36

 TotSSq  =10.3246
 RegSSq  = 7.7706
 ResSSq  = 2.5541
 CO      = 0.2477
 DIR     = 0.8288
 PERI    = 0.0860
 SUBSEQ  = 2.0941
 SEQ     = 4.5149
 check   = 7.7715

//      ++++++++++++++++++++++++++++++++++++++++++++++++++++++++++++++++++++
//      Using Sequences 1,2,5 and 6, which make up a SBURMD.
//      The y variate corresponds to these sequences and is again
//      log(food intake)
//
//      Linear Model:
//       log(y)= g.m + sequence + sequence(subj) + period + direct + resid
//
//      Treatment Sequences: S S S S P P P P
//                           S S P P S S P P
//                           P P P P S S S S
//                           P P S S P P S S
//
Z = [X(1:16,1:5) X(1:16,10:17)];
ZZ= [X(33:48,1:5) X(33:48,10:17)];
X = [ Z ; ZZ ];

y = [y(1:16,:) ; y(33:48,:)];

exec('Anova2.mat');
```

```
X'*X
   32    0    0    0    0    0    0    0    0    0    0    0    0
    0   16    8    8    0    0    0    0    0    0    0    0    0
    0    8   16    8    0    0    0    0    0    0    0    0    4
    0    8    8   16    0    0    0    0    0    0    0    0    4
    0    0    0    0    8    0    0    0    0    0    0    0    0
    0    0    0    0    0    8    0    0    0    0    0    0    0
    0    0    0    0    0    0    8    0    0    0    0    0    0
    0    0    0    0    0    0    0    8    0    0    0    0    0
    0    0    0    0    0    0    0    0   16    8    8    0    0
    0    0    0    0    0    0    0    0    8   16    8    0    0
    0    0    0    0    0    0    0    0    8    8   16    0    0
    0    0    0    0    0    0    0    0    0    0    0   32    0
    0    0    4    4    0    0    0    0    0    0    0    0   24

 TotSSq  =7.8053
 RegSSq  =6.4607
 ResSSq  =1.3447
 CO      =0.3132
 DIR     =0.4398
 PERI    =0.1260
 SUBSEQ  =1.0732
 SEQ     =4.1107
 chec    =6.0628
```

Appendix N: Reprint of Paper by Pattison and Street (1990)

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Small Non-Isomorphic Repeated Measurements Designs

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Abstract

Over the last few years a number of authors have investigated the structure of optimal repeated measurements designs. Various constructions for such designs have been given. In this paper we consider the construction of non-isomorphic optimal repeated measurements designs when t=2 and 3.

1. Introduction

In a *repeated measurements design* (RMD) there are t treatments, n experimental units and the experiment lasts for p periods. Each experimental unit receives one treatment during each period. Thus the design may be represented as a pxn array containing entries from {1,2,...,t}. Examples of RMDs with t=2, p=4 and n=4 appear in Table 1.

1	1	2	2	1	1	1	2
2	2	1	1	1	2	2	1
1	1	2	2	2	2	2	1
2	2	1	1	2	1	1	1
(a)				(b)			

Table 1. *Examples of RMDs.*

A RMD is said to be *uniform on units* (or columns) if each treatment appears the same number of times in each column, and to be *uniform on periods* (or rows) if each treatment appears the same number of times in each row. A RMD is said to be *uniform* if it is uniform on both units and periods. Thus, in a uniform RMD, each treatment appears p/t times in each column and n/t times in each row. Hence necessary conditions for the existence of uniform RMDs are t|p and t|n. The design (a) in Table 1 is a uniform RMD, whereas design (b) is not uniform on either rows or columns.

Let m_{ij} denote the number of times that treatment i is preceded by treatment j. A

RMD is said to be *balanced* if

$$m_{ij} = (1-\delta_{ij})\,\frac{n(p-1)}{t(t-1)}, \quad 1 \le i,j \le t,$$

where δ_{ij} is the Kronecker δ, and to be *strongly balanced* if

$$m_{ij} = \frac{n(p-1)}{t^2}, \quad 1 \le i,j \le t.$$

The design (a) in Table 1 is balanced and design (b) is strongly balanced.

The linear models associated with these designs have been given by a number of authors (see, for example, Cheng and Wu (1980), Kunert (1984) and Street (1988)). Cheng and Wu (1980) have shown that one class of optimal designs are the strongly balanced, uniform RMDs and they give a construction for such designs when $n=t^2$ and $p=2t$. Placing two such designs side-by-side gives a strongly balanced, uniform design with $n=2t^2$ and $p=2t$, and placing two of their designs one under the other gives a strongly balanced, uniform RMD with $n=t^2$ and $p=2(2t)$. (These are examples of pasting constructions.) Thus, in general, there are strongly balanced, uniform RMDs with $n=\lambda_1 t^2$, $\lambda_1 \ge 1$, and $p=2\lambda_2 t$, $\lambda_2 \ge 1$ for all t. The design (a) in Table 2 is the strongly balanced, uniform RMD for t=2, p=4, n=4 from the construction of Cheng and Wu (1980). The designs (b) and (c) show strongly balanced, uniform RMD obtained from (a) by horizontal and vertical pasting respectively.

(a)

1	1	2	2
1	2	1	2
2	2	1	1
2	1	2	1

(b)

1	1	1	1	2	2	2	2
1	1	2	2	1	1	2	2
2	2	2	2	1	1	1	1
2	2	1	1	2	2	1	1

(c)

1	1	2	2
1	2	1	2
2	2	1	1
2	1	2	1
1	1	2	2
1	2	1	2
2	2	1	1
2	1	2	1

Table 2. *Examples of horizontal and vertical pasting.*

Sen and Mukerjee (1987) have shown how to construct a strongly balanced, uniform RMD for $n=t^2$ and $p=3t$. As their construction uses two mutually orthogonal Latin squares (MOLS) of size t, it can only be used when there are at least 3 treatments (and $t \neq 6$).

We are interested in the total number of strongly balanced, uniform RMDs and ways of constructing all these designs for small values of t and p for varying n. In the remainder of this paper, we consider the construction of non-isomorphic, strongly balanced, uniform RMDs for the cases t=2,p=4; t=2,p=6; t=2,p even,p>6 and t=3,p=6.

2. The Case t=2 and p=4 (=2t)

In this case, the necessary conditions for the existence of strongly balanced, uniform RMDs are 2|4, 2|n and 4|3n. Thus, n=4s, s≥1. Since the designs are uniform on units (or columns), each column of the array must contain two 1's and two 2's. Hence each experimental unit must receive one of six possible sequences. These are listed in Table 3.

Sequence	S_1	S_2	S_3	S_4	S_5	S_6
Period 1	1	1	1	2	2	2
2	1	2	2	1	1	2
3	2	1	2	1	2	1
4	2	2	1	2	1	1

Table 3. *All sequences of length 4 containing two 1's and two 2's.*

For each sequence we have also recorded, in Table 4, the number of times the ordered pairs of treatments (1,1), (1,2), (2,1) and (2,2), appear on adjacent periods.

Sequence	S_1	S_2	S_3	S_4	S_5	S_6
$(1,1)^T$	1	0	0	1	0	1
$(1,2)^T$	1	2	1	1	1	0
$(2,1)^T$	0	1	1	1	2	1
$(2,2)^T$	1	0	1	0	0	1

Table 4. *The number of times the ordered pairs appear in each sequence.*

We let x_i, i=1, 2,...,6, be the number of units receiving treatment sequence S_i in the design. Then, counting experimental units and using the fact that the design is both strongly balanced and uniform in rows (periods), we get the following equations.

$$
\begin{aligned}
x_1 + x_2 + x_3 + x_4 + x_5 + x_6 &= n = 4s,\\
x_1 + x_4 + x_6 &= (p-1)n/t^2 = 3n/4 = 3s,\\
x_1 + 2x_2 + x_3 + x_4 + x_5 &= 3s,\\
x_2 + x_3 + x_4 + 2x_5 + x_6 &= 3s,\\
x_1 + x_3 + x_6 &= 3s,\\
x_1 + x_2 + x_3 &= n/t = n/2 = 2s,\\
x_1 + x_4 + x_5 &= 2s,\\
x_2 + x_4 + x_6 &= 2s,\\
x_3 + x_5 + x_6 &= 2s.
\end{aligned}
$$

Solving, we get

$$x_1 = x_6 = x_2 + s,$$
$$x_2 = x_5,$$
$$x_3 = x_4 = s - 2x_2,$$
$$0 \le x_2 \le \left[\frac{s}{2}\right],\ s=1,2,3,...,$$

where $\left[\frac{s}{2}\right]$ is the largest integer less than or equal to s/2.

We summarise these results in the following theorem.

Theorem 1

When t=2 and p=4, all strongly balanced, uniform RMDs have n=4s units, s=1,2,... . There are $\left[\frac{s}{2}\right]$ + 1 non-isomorphic designs with 4s units and these designs have $a+s$ sequences of type S_1, and of type S_6, a sequences of type S_2, and of type S_5, and $s-2a$ sequences of type S_3, and of type S_4, where a =0,1,2,..., $\left[\frac{s}{2}\right]$. All the designs have (1,2) as an automorphism. □

In fact, all the designs are obtained by taking appropriate combinations of the design $(x_1,x_2,x_3) = (1,0,1)$ when n=4 and the design $(x_1,x_2,x_3) = (3,1,0)$ when n=8. This can be seen from Table 5 where all strongly balanced, uniform RMDs for n=4,8,12,16 and 20 are given. The designs constructed by Cheng and Wu (1980) correpsond to the case a =0 of the theorem.

n=4

1 1 2 2
1 2 1 2
2 2 1 1
2 1 2 1

n=8

1 1 1 1 2 2 2 2
1 1 2 2 2 1 1 2
2 2 2 2 2 1 1 1 1
2 2 1 1 2 2 1 1

1 1 1 1 2 2 2 2
1 1 1 2 1 2 2 2
2 2 2 1 2 1 1 1
2 2 2 2 2 1 1 1 1

n=12

1 1 1 1 1 1 2 2 2 2 2 2
1 1 1 2 2 2 1 1 1 2 2 2
2 2 2 2 2 2 1 1 1 1 1 1 1
2 2 2 1 1 1 2 2 2 1 1 1

1 1 1 1 1 1 2 2 2 2 2 2
1 1 1 1 2 2 1 1 2 2 2 2
2 2 2 2 1 2 1 2 1 1 1 1
2 2 2 2 2 1 2 1 1 1 1 1

n=16

1 1 1 1 1 1 1 1 2 2 2 2 2 2 2 2
1 1 1 1 2 2 2 2 1 1 1 1 2 2 2 2
2 2 2 2 2 2 2 2 1 1 1 1 1 1 1 1
2 2 2 2 1 1 1 1 2 2 2 2 1 1 1 1

1 1 1 1 1 1 1 1 2 2 2 2 2 2 2 2
1 1 1 1 1 1 2 2 2 1 1 1 2 2 2 2
2 2 2 2 2 1 2 2 1 1 2 1 1 1 1 1
2 2 2 2 2 2 1 1 2 2 1 1 1 1 1 1

1 1 1 1 1 1 1 1 2 2 2 2 2 2 2 2
1 1 1 1 1 1 2 2 1 1 2 2 2 2 2 2
2 2 2 2 2 1 1 2 2 1 1 2 2 2 2 2
2 2 2 2 2 2 2 1 1 2 2 1 1 1 1 1

n=20

1 1 1 1 1 1 1 1 1 1 2 2 2 2 2 2 2 2 2 2
1 1 1 1 1 2 2 2 2 2 1 1 1 1 1 2 2 2 2 2
2 2 2 2 2 2 2 2 2 2 1 1 1 1 1 1 1 1 1 1
2 2 2 2 2 1 1 1 1 2 2 2 2 2 1 1 1 1 1 1

1 1 1 1 1 1 1 1 1 1 2 2 2 2 2 2 2 2 2 2
1 1 1 1 1 1 2 2 2 2 1 1 1 1 2 2 2 2 2 2
2 2 2 2 2 1 2 2 2 1 1 1 2 1 1 1 1 1 1 1
2 2 2 2 2 2 1 1 1 2 2 2 1 1 1 1 1 1 1 1

1 1 1 1 1 1 1 1 1 1 2 2 2 2 2 2 2 2 2 2
1 1 1 1 1 1 2 2 2 1 1 1 2 2 2 2 2 2 2 2
2 2 2 2 2 1 1 2 1 2 2 1 1 1 1 1 1 1 1 1
2 2 2 2 2 2 1 1 2 1 1 2 2 2 2 2 2 2 2 2

1 1 1 1 1 1 1 1 1 1 2 2 2 2 2 2 2 2 2 2
1 1 1 1 1 1 2 2 2 1 1 1 2 2 2 2 2 2 2 2
2 2 2 2 2 1 1 2 1 2 2 1 1 1 1 1 1 1 1 1
2 2 2 2 2 2 1 1 2 1 1 2 2 2 2 2 2 2 2 2

Table 5. *All strongly balanced, uniform RMDs for t=2, p=4 and n=4,8,12,16 and 20.*

3. The case t=2 and p=6 (=3t)

Here the necessary conditions for the existence of strongly balanced, uniform RMDs are 2|6, 2|n and 4|5n, so again n=4s, s ≥ 1. There are now twenty possible sequences, each containing three 1's and three 2's. They are listed in Table 6.

Sequence		S_1	S_2	S_3	S_4	S_5	S_6	S_7	S_8	S_9	S_{10}	S_{11}	S_{12}	S_{13}	S_{14}	S_{15}	S_{16}	S_{17}	S_{18}	S_{19}	S_{20}
Period	1	1	1	1	1	1	1	1	1	1	1	2	2	2	2	2	2	2	2	2	2
	2	1	1	1	1	2	2	2	2	2	2	1	1	1	1	1	1	2	2	2	2
	3	1	2	2	2	1	1	2	1	2	2	1	1	2	1	2	2	1	1	1	2
	4	2	1	2	2	1	2	1	2	1	2	1	2	1	2	1	2	1	1	2	1
	5	2	2	1	2	2	1	1	2	2	1	2	1	1	2	2	1	1	2	1	1
	6	2	2	2	1	2	2	2	1	1	1	2	2	2	1	1	1	2	1	1	1

Table 6. *All sequences of length 6 containing three 1's and three 2's.*

For each sequence, the number of times that the ordered pairs of treatments (1,1), (1,2), (2,1) and (2,2) appear on adjacent periods, are recorded in Table 7.

Sequence	S_1	S_2	S_3	S_4	S_5	S_6	S_7	S_8	S_9	S_{10}	S_{11}	S_{12}	S_{13}	S_{14}	S_{15}	S_{16}	S_{17}	S_{18}	S_{19}	S_{20}
$(1,1)^T$	2	1	1	1	1	0	1	0	0	1	2	1	1	1	0	1	2	1	1	2
$(1,2)^T$	1	2	2	1	2	3	2	2	2	1	1	2	2	1	2	1	1	1	1	0
$(2,1)^T$	0	1	1	1	1	2	1	2	2	1	1	2	2	2	3	2	1	2	2	1
$(2,2)^T$	2	1	1	2	1	0	1	1	1	2	1	0	0	1	0	1	1	1	1	2

Table 7. *The number of times the ordered pairs (1,1), (1,2), (2,1), (2,2) appear in each sequence.*

We let x_i, i=1,2,..,20, be the number of units receiving treatment sequence S_i in the design. Then we can obtain the following equations in a similar way to those of the previous case , using the fact that the design is both strongly balanced and uniform on rows (periods).

$$2x_1+x_2+x_3+x_4+x_5+x_7+x_{10}+2x_{11}+x_{12}+x_{13}+x_{14}+x_{16}+2x_{17}+x_{18}+x_{19}+2x_{20} = \frac{(p-1)n}{t^2} = 5s,$$
$$x_1+2x_2+2x_3+x_4+2x_5+3x_6+2x_7+2x_8+2x_9+x_{10}+x_{11}+2x_{12}+2x_{13}+x_{14}+2x_{15}+x_{16}+x_{17}+x_{18}+x_{19} = 5s,$$
$$x_2+x_3+x_4+x_5+2x_6+x_7+2x_8+2x_9+x_{10}+x_{11}+2x_{12}+2x_{13}+2x_{14}+3x_{15}+2x_{16}+x_{17}+2x_{18}+2x_{19}+x_{20} = 5s,$$
$$2x_1+x_2+x_3+2x_4+x_5+x_7+x_8+x_9+2x_{10}+x_{11}+x_{14}+x_{16}+x_{17}+x_{18}+x_{19}+2x_{20} = 5s,$$

$$x_1 + x_2 + x_3 + x_4 + x_5 + x_6 + x_7 + x_8 + x_9 + x_{10} = \frac{n}{t} = 2s,$$
$$x_1 + x_2 + x_3 + x_4 + x_{11} + x_{12} + x_{13} + x_{14} + x_{15} + x_{16} = 2s,$$
$$x_1 + x_5 + x_6 + x_8 + x_{11} + x_{12} + x_{14} + x_{17} + x_{18} + x_{19} = 2s,$$
$$x_2 + x_5 + x_7 + x_9 + x_{11} + x_{13} + x_{15} + x_{17} + x_{18} + x_{20} = 2s,$$
$$x_3 + x_6 + x_7 + x_{10} + x_{12} + x_{13} + x_{16} + x_{17} + x_{19} + x_{20} = 2s,$$
$$x_4 + x_8 + x_9 + x_{10} + x_{14} + x_{15} + x_{16} + x_{18}\ x_{19} + x_{20} = 2s.$$

Solving these equations, we find that

$$x_1 = x_7 + x_9 + x_{10} + x_{13} + x_{15} + x_{16} + x_{17} + x_{18} + x_{19} + 2x_{20} - 2s,$$
$$x_2 = x_7 + 2x_{10} - x_{15} + x_{16} + 2x_{17} + x_{18} + 2x_{19} + 3x_{20} - 3s,$$
$$x_3 = -2x_7 + x_8 - 2x_{10} - x_{13} - x_{14} + x_{15} - x_{16} - 2x_{17} - x_{19} - 3x_{20} + 3s,$$
$$x_4 = -x_8 - x_9 - x_{10} - x_{14} - x_{15} - x_{16} - x_{18} - x_{19} - x_{20} + 2s,$$
$$x_5 = -2x_7 - x_9 - 2x_{10} + x_{12} + x_{14} + x_{15} - 2x_{17} - x_{18} - x_{19} - 3x_{20} + 3s,$$
$$x_6 = x_7 - x_8 + x_{10} - x_{12} - x_{14} - x_{15} + x_{17} + 2x_{20} - s,$$
$$x_{11} = -x_{12} - x_{13} - x_{14} - x_{15} - x_{16} - x_{17} - x_{18} - x_{19} - x_{20} + 2s,$$

$0 \le x_7, x_8, x_9, x_{10}, x_{12}, x_{13}, x_{14}, x_{15}, x_{16}, x_{17}, x_{18}, x_{19}, x_{20} \le 2s$, s = 1,2,3,... .

In the previous section, we could find all strongly balanced, uniform RMDs from the equivalent equations. Here we cannot find all solutions to the above equations very easily. When s is any integer value then the set of solutions to the above equations are a module which is finitely generated. The RMDs correspond to the positive elements of the module (De Launey (1989)). However, the basis of the module may only be expressible as linear combinations of the original x_i's. Hence this observation does not appear to make the task of finding the designs any easier.

It is no longer true that all solutions have (1,2) as an automorphism. Those that do are called *symmetric* designs. Otherwise, we say that the design is *non-symmetric*. In a symmetric design $x_1=x_{20}, x_2=x_{19},...,x_{10}=x_{11}$.

All non-isomorphic strongly balanced, uniform RMDs with t=2, p=6 and n=4, are given in Table 8. We see that there are 15 designs, of which the first 10 are symmetric.

1 1 2 2	1 1 2 2	1 1 2 2	1 1 2 2	1 1 2 2	
1 2 1 2	1 2 1 2	1 1 2 2	1 2 1 2	1 1 2 2	
1 1 2 2	1 2 1 2	2 2 1 1	2 2 1 1	2 2 1 1	
2 2 1 1	2 1 2 1	1 2 1 2	1 2 1 2	2 2 1 1	
2 2 1 1	2 2 1 1	2 2 1 1	2 1 2 1	1 2 1 2	
2 1 2 1	2 1 2 1	2 1 2 1	2 1 2 1	2 1 2 1	
1 1 2 2	1 1 2 2	1 1 2 2	1 1 2 2	1 1 2 2	*symmetric*
1 2 1 2	1 2 1 2	1 2 1 2	2 2 1 1	2 2 1 1	
2 2 1 1	2 1 2 1	2 2 1 1	1 2 1 2	2 2 1 1	
2 2 1 1	2 1 2 1	2 1 2 1	1 2 1 2	1 2 1 2	
1 1 2 2	2 2 1 1	2 1 2 1	2 1 2 1	1 1 2 2	
2 1 2 1	1 2 1 2	1 2 1 2	2 1 2 1	2 1 2 1	
1 1 2 2	1 1 2 2	1 1 2 2	1 1 2 2	1 1 2 2	
1 2 1 2	1 2 1 2	1 2 1 2	1 2 1 2	1 2 1 2	
1 2 2 1	1 2 2 1	1 2 2 1	1 2 2 1	2 2 1 1	
2 1 2 1	2 1 2 1	2 2 1 1	2 2 1 1	1 2 2 1	*non-symmetric*
2 1 1 2	2 2 1 1	2 1 1 2	2 1 2 1	2 1 2 1	
2 2 1 1	2 1 1 2	2 1 2 1	2 1 1 2	2 1 1 2	

Table 8. *Strongly balanced, uniform RMD's for t=2, p=6, n=4.*

The number of non-isomorphic (symmetric and non-symmetric), strongly balanced, uniform RMDs with t=2, p=6 and n=4,8 and 12, are given in Table 9.

n	4	8	12
symmetric	10	84	388
non-symmetric	5	130	1636
Total	15	214	2024

Table 9. *The number of non-isomorphic strongly balanced, uniform RMDs for t=2 and p=6.*

When t=2 and p=4, design with n=4s, s≥3, are obtained by horizontally pasting an appropriate number of designs with n=4 and n=8, and they can be obtained in no other way. This is no longer the case when t=2 and p=6. Table 10 shows the number of designs with n=8 which can be obtained by horizontally pasting designs with n=4. (We used all 20 designs with n=4 - the 10 symmetric and 5 non-symmetric designs from Table 8, and the 5 designs obtained from the non-symmetric designs by applying the permutation

(12).) Table 10 also gives the number of designs with n=12 which can be obtained by horizontally pasting a design with n=4 and one with n=8 (84 symmetric, 130 non-symmetric and 130 non-symmetric permuted (1,2)).

n	8	12
symmetric	51	380
non-symmetric	75	1494
Total	126	1874

Table 10. *The number of non-isomorphic, strongly balanced, uniform RMDs possible using pasting for n=8 and 12.*

Non-symmetric designs permuted by (1 2) are included for pasting as they may lead to designs which cannot be obtained otherwise. Table 11 gives a design for n=8 which is obtained by horizontally pasting a non-symmetric design for n=4 with 1 and 2 interchanged and a n=4 design from Table 8. This design cannot be obtained by pasting any two designs in Table 8. For n=8 there are 12 such strongly balanced, uniform RMDs, two of which are symmetric.

1	1	2	2	:	2	2	1	1
1	2	1	2	:	2	1	2	1
1	2	2	1	:	2	1	1	2
2	1	2	1	:	1	2	1	2
2	1	1	2	:	1	2	2	1
2	2	1	1	:	1	1	2	2

Table 11. *A strongly balanced, uniform RMD for t=2, p=6 and n=8 pasted from a non-symmetric design with the non-symmetric design permuted by (12).*

Pasting doesn't lead us to all designs: For n=8 there are 88 'new' designs which cannot be obtained from n=4 designs and for n=12, there are 150 'new' designs.

4. The Case t=2 and p>6 (even)

In this section we describe another recursive construction for strongly balanced uniform RMDs. Using Theorem 2 it is possible to construct such designs for t=2, n=4s and p=8,10,12,... .

Theorem 2

Let D_1 be a strongly balanced, uniform RMD with t=2, $p=p_1$ and n units, and let D_2 be a strongly balanced, uniform RMD with t=2, $p=p_2$ and n units. Then there is a strongly balanced, uniform RMD with t=2, $p=p_1+p_2$ and n units.

Proof

We can permute the columns of D_1 so that the first n/2 columns have a 1 in the final row (and hence the remaining columns have a 2 in the final row). We can permute the columns of D_2 so that the first n/4 columns begin with 1, the next n/4 columns begin with 2, the next n/4 columns begin with 1 and the final n/4 columns begin with 2. The required design is

$$D_3 = \begin{bmatrix} D_1 \\ D_2 \end{bmatrix}.$$

Clearly D_3 has t=2, $p=p_1+p_2$ and there are n units. D_3 is uniform in rows and columns because D_1 and D_2 were. What are the values of m_{ij} in D_3? From D_1 and D_2 and the method of construction we have that

$$m_{ij} = \frac{n(p_1-1)}{4} + \frac{n(p_2-1)}{4} + \frac{n}{4} = \frac{n(p_1-1+p_2-1+1)}{4},$$

as required. □

The designs in Table 12 illustrate this construction. The first is a t=2, p=8, n=8 design obtained from two (different) designs with t=2, p=4, n=8. The second is a design with t=2, p=10, n=4 obtained from designs with t=2, p=6, n=4 and t=2, p=4, n=4. The third design has t=2, p=12, n=4 and is obtained from two (different) designs with t=2, p=6, n=4.

(a)
2 2 2 2 1 1 1 1
1 2 2 2 1 1 1 2
2 1 1 1 2 2 2 1
1 1 1 1 2 2 2 2

1 1 2 2 1 1 2 2
1 1 1 1 2 2 2 2
2 2 1 1 2 2 1 1
2 2 2 2 1 1 1 1

(b)
2 2 1 1
1 2 1 2
2 1 1 2
2 1 2 1
1 2 2 1
1 1 2 2

1 2 1 2
1 1 2 2
2 1 2 1
2 2 1 1

(c)
1 2 1 2
2 1 2 1
2 1 2 1
2 2 1 1
1 2 1 2
1 1 2 2

1 2 1 2
1 1 2 2
2 1 2 1
1 2 2 1
2 2 1 1
2 1 1 2

Table 12. *Strongly balanced, uniform RMDs obtained by vertical pasting.*

5. The Case t=3 and p=6 (=2t)

Once we have more than two treatments, the situation rapidly becomes much more complicated. We illustrate some of these difficulties by considering the case t=3 and p=6.

There are now 90 sequences of length 6 which contain two 1's, two 2's and two 3's. These can be grouped into 15 sets of 6 sequences each, where sequences in a set can be obtained from each other by applying a permutation of 1,2 and 3 (that is, an element of S_3).

The 90 sequences, grouped into the 15 sets of 6, together with a label for each sequence, appear in Table 13.

	1 1 2 2 3 3 s_{11}	1 1 2 3 2 3 s_{21}	1 1 2 3 3 2 s_{31}
(12)	2 2 1 1 3 3 s_{12}	2 2 1 3 1 3 s_{22}	2 2 1 3 3 1 s_{32}
(13)	3 3 2 2 1 1 s_{13}	3 3 2 1 2 1 s_{23}	3 3 2 1 1 2 s_{33}
(23)	1 1 3 3 2 2 s_{14}	1 1 3 2 3 2 s_{24}	1 1 3 2 2 3 s_{34}
(123)	2 2 3 3 1 1 s_{15}	2 2 3 1 3 1 s_{25}	2 2 3 1 1 3 s_{35}
(132)	3 3 1 1 2 2 s_{16}	3 3 1 2 1 2 s_{26}	3 3 1 2 2 1 s_{36}
	1 2 1 2 3 3 s_{41}	1 2 1 3 2 3 s_{51}	1 2 1 3 3 2 s_{61}
(12)	2 1 2 1 3 3 s_{42}	2 1 2 3 1 3 s_{52}	2 1 2 3 3 1 s_{62}
(13)	3 2 3 2 1 1 s_{43}	3 2 3 1 2 1 s_{53}	3 2 3 1 1 2 s_{63}
(23)	1 3 1 3 2 2 s_{44}	1 3 1 2 3 2 s_{54}	1 3 1 2 2 3 s_{64}
(123)	2 3 2 3 1 1 s_{45}	2 3 2 1 3 1 s_{55}	2 3 2 1 1 3 s_{65}
(132)	3 1 3 1 2 2 s_{46}	3 1 3 2 1 2 s_{56}	3 1 3 2 2 1 s_{66}
	1 2 2 1 3 3 s_{71}	1 2 3 1 2 3 s_{81}	1 2 3 1 3 2 s_{91}
(12)	2 1 1 2 3 3 s_{72}	2 1 3 2 1 3 s_{82}	2 1 3 2 3 1 s_{92}
(13)	3 2 2 3 1 1 s_{73}	3 2 1 3 2 1 s_{83}	3 2 1 3 1 2 s_{93}
(23)	1 3 3 1 2 2 s_{74}	1 3 2 1 3 2 s_{84}	1 3 2 1 2 3 s_{94}
(123)	2 3 3 2 1 1 s_{75}	2 3 1 2 3 1 s_{85}	2 3 1 2 1 3 s_{95}
(132)	3 1 1 3 2 2 s_{76}	3 1 2 3 1 2 s_{86}	3 1 2 3 2 1 s_{96}
	1 2 2 3 1 3 $s_{10,1}$	1 2 3 2 1 3 $s_{11,1}$	1 3 2 2 1 3 $s_{12,1}$
(12)	2 1 1 3 2 3 $s_{10,2}$	2 1 3 1 2 3 $s_{11,2}$	2 3 1 1 2 3 $s_{12,2}$
(13)	3 2 2 1 3 1 $s_{10,3}$	3 2 1 2 3 1 $s_{11,3}$	3 1 2 2 3 1 $s_{12,3}$
(23)	1 3 3 2 1 2 $s_{10,4}$	1 3 2 3 1 2 $s_{11,4}$	1 2 3 3 1 2 $s_{12,4}$
(123)	2 3 3 1 2 1 $s_{10,5}$	2 3 1 3 2 1 $s_{11,5}$	2 1 3 3 2 1 $s_{12,5}$
(132)	3 1 1 2 3 2 $s_{10,6}$	3 1 2 1 3 2 $s_{11,6}$	3 2 1 1 3 2 $s_{12,6}$
	1 2 2 3 3 1 $s_{13,1}$	1 2 3 2 3 1 $s_{14,1}$	1 2 3 3 2 1 $s_{15,1}$
(12)	2 1 1 3 3 2 $s_{13,2}$	2 1 3 1 3 2 $s_{14,2}$	2 1 3 3 1 2 $s_{15,2}$
(13)	3 2 2 1 1 3 $s_{13,3}$	3 2 1 2 1 3 $s_{14,3}$	3 2 1 1 2 3 $s_{15,3}$
(23)	1 3 3 2 2 1 $s_{13,4}$	1 3 2 3 2 1 $s_{14,4}$	1 3 2 2 3 1 $s_{15,4}$
(123)	2 3 3 1 1 2 $s_{13,5}$	2 3 1 3 1 2 $s_{14,5}$	2 3 1 1 3 2 $s_{15,5}$
(132)	3 1 1 2 2 3 $s_{13,6}$	3 1 2 1 2 3 $s_{14,6}$	3 1 2 2 1 3 $s_{15,6}$

Table 13. *90 possible sequences for t=3 and p=6.*

Suppose there are x_{ij} units receiving treatment sequence S_{ij} in the final design. Then uniformity in rows gives us 3x6 = 18 equations and the strongly balanced property gives us a further 9 equations. However, the equations are not independent (for instance as there can only be 1's, 2's and 3's in each row, once the number of 1's and 2's are known, the number of 3's is also). The 27 equations in fact have rank 15 and involve 90 unknown x_{ij}.

We simplify the problem further by finding only those designs for which all the elements of S_3 are an automorphism. Thus n=18s and there are two independent equations that the 15 unknowns must satisfy.

Let x_i be the number of sequences of type S_{i1} in the final design.

Then

$$\sum_{i=1}^{15} x_i = n/6 = 3s \qquad (1)$$

$$6x_1 + 2x_2 + 4x_3 + 2x_4 + 2x_6 + 4x_7 + 2x_{10} + 2x_{12} + 4x_{13} + 2x_{15} = \frac{5n}{9} = 10s \qquad (2)$$

$$2x_1+4x_2+3x_3+4x_4+5x_5+4x_6+3x_7+5x_8+5x_9+4x_{10}+5x_{11}+4x_{12}+3x_{13}+5x_{14}+4x_{15} = 10s \qquad (3)$$

In attempting to find solutions it appears to be easiest to work with the original equations.

Theorem 3

There are 72 non-isomorphic, strongly balanced, uniform RMDs with t=3, p=6, n=18 and with S_3 as an automorphism group.

Proof

Any such design must satisfy the equations (1), (2) and (3) with s=1. Thus $0 \le x_i \le 3$. But if any $x_i = 3$, then either equation (2) or (3) is contradicted. If x_5, x_8, x_9, x_{11} or $x_{14} = 2$, then (1) and (3) can not hold simultaneously. If $x_1 = 2$, then equation (2) is false.

If $x_1 = 1$, then either one of x_3, x_7 and x_{13} is 1 and one of x_5, x_8, x_9, x_{11} and x_{14} is 1, or two of x_2, x_4, x_6, x_{10}, x_{12}, x_{15} is 1, or one of x_2, x_4, x_6, x_{10}, x_{12} and x_{15} is 2. This gives 3 x 5 + 15 + 6 = 36 designs.

If $x_1 = 0$, then either one of x_3, x_7 and x_{13} is 2 and one of x_2, x_4, x_6, x_{10}, x_{12} and x_{15} is 1 or two of x_3, x_7 and x_{13} are 1 and one of x_2, x_4 x_6, x_{10}, x_{12} and x_{15} is 1. This gives 3 x 6 + 3 x 6 = 36 designs. The result follows. □

Similar counting shows that there are 1677 such designs when n=36 (s=2).

5. Summary

In this paper we have produced constructions for all strongly balanced, uniform RMDs for t=2, p=4 and n=4s. All strongly balanced, uniform RMDs for t=2, p=6 and n=4 have been given from which we can horizontally paste to produce some t=2, p=6 and n=4s designs. Using t=2, p=4, 6 and n=4s we can construct t=2, p>6 (even) and n=4s strongly balanced, uniform RMDs using vertical pasting. For t=3, p=6 and n=18, 36 we have counted the number of strongly balanced, uniform RMDs that have elements of S_3 as an automorphism.

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